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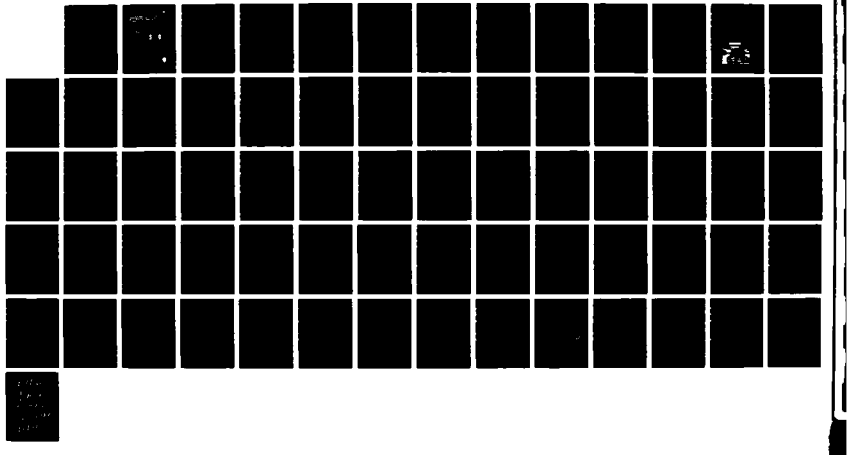

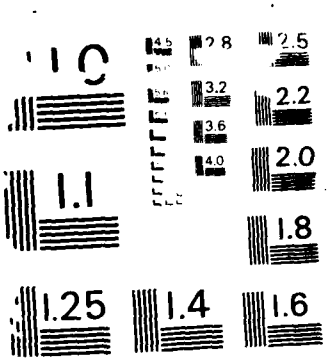

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LONG-TERM BIOEFFECTS OF 435-MHz RADIOFREQUENCY RADIATION ON SELECTED BLOOD-BORNE ENDPOINTS IN CANNULATED RATS

Volume 6. Cardiovascular Studies

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USAF SCHOOL OF AEROSPACE MEDICINE
Human Systems Division (AFSC)
Brooks Air Force Base, TX 78235-5301

NOTICES

This final report was submitted by Georgia Tech Research Institute, Georgia Institute of Technology, Atlanta, Georgia, under contract F33615-83-K-0600, job order 7757-01-78, with the USAF School of Aerospace Medicine, Human Systems Division, AFSC, Brooks Air Force Base, Texas. James H. Merritt (USAFSAM/RZP) was the Laboratory Project Scientist-in-Charge.

When Government drawings, specifications, or other data are used for any purpose other than in connection with a definitely Government-related procurement, the United States Government incurs no responsibility nor any obligation whatsoever. The fact that the Government may have formulated or in any way supplied the said drawings, specifications, or other data, is not to be regarded by implication, or otherwise in any manner construed, as licensing the holder, or any other person or corporation; or as conveying any rights or permission to manufacture, use, or sell any patented invention that may in any way be related thereto.

The animals involved in this study were procured, maintained, and used in accordance with the Animal Welfare Act and the "Guide for the Care and Use of Laboratory Animals" prepared by the Institute of Laboratory Animal Resources-National Research Council.

The Office of Public Affairs has reviewed this report, and it is releasable to the National Technical Information Service, where it will be available to the general public, including foreign nationals.

This report has been reviewed and is approved for publication.

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Two hundred adult male white rats (Sprague-Dawley, CAMM Labs) with chronically implanted aortic cannulas were randomly divided into 2 groups. Animals in the first group were exposed to low-level (1.0 mW/cm^2) pulsed-wave 435-MHz radiofrequency radiation for approximately 22 hours daily, 7 days a week, for 6 months. Animals in the second group were maintained under identical conditions but were not radiated. The cannulas were used to record heart rate and arterial blood pressure in unrestrained, unanesthetized rats. Statistical analysis of the results did not indicate any increase in heart rate or arterial blood pressure of RFR-exposed animals when compared to sham-exposed animals. Thus, chronic exposure to the low-level radiofrequency environment did not induce stress that was manifested as increases in heart rate or mean arterial blood pressure. This result correlated with the conclusion of a previous report demonstrating no RFR effects on plasma norepinephrine and epinephrine concentrations in the group of rats.

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I. INTRODUCTION

Relatively little is known regarding the response of mammalian heart rate and arterial blood pressure to nonionizing radiation. Some investigators have found decreases in heart rate and in arterial blood pressure during acute microwave exposure [1,2,3], but others have not [4,5]. Knowledge of effects induced by exposure to chronic low-level microwave radiation is even more sparse.

Exposure to nonionizing radiation increases mammalian body temperature. This increase depends on both the exposure intensity and duration. Sometimes the temperature increase is so small that it can not be detected with available temperature sensors and instrumentation. An illustration of this difficulty in accurately assessing body temperature can be seen during the early stages of radiofrequency radiation (RFR) hyperthermia, when blood flow to the colonic and rectal regions (where body temperature is most commonly measured) lags behind blood flow to other regions. Thus, rectal temperature increases by 0.05 to 0.10 ^{o}C (an increase that is hard to detect), while body temperature exceeds rectal temperature by 0.5 ^{o}C or more [6]. Nevertheless, the increase is present and affects both animal metabolism and circulation in either a general or local way. Exposure to intense nonionizing RFR fields probably increases cardiac output (measurements of cardiac output during RFR exposure are not cited in the literature). The increase in body temperature due to intense RFR exposure would induce local or even general vasodilation, leading to a decrease in mean arterial blood pressure and subsequent sympathetic adrenergic stimulation. These mechanisms would provoke increased heart rate and (possibly) increased filling of the heart during diastole, which in turn would lead to increased cardiac output. Thus, heart rate would increase above normal while mean arterial blood pressure remained unchanged or slightly increased.

Exposure of mammals to low-intensity RFR might induce only local circulatory changes while heart rate and arterial blood pressure remain unchanged. It is unlikely that low-level RFR exposure in a relatively stress-

free environment would preferentially affect the autonomic nervous system. Effects of RFR exposure on the autonomic nervous system as reported by Presman [7] were observed under higher power densities and would thus not be considered "low-level" exposures. Therefore, one would not expect the arterial blood pressure to increase after chronic low-level microwave exposure. We have already shown that chronic (several months) low-level RFR exposure of rats does not change the resting concentration of plasma catecholamines [8] or of adrenocorticotropic hormone (ACTH), corticosterone or prolactin [9,10].

This study was undertaken in part to determine whether chronic low-level microwave exposure had any effect on the cardiovascular parameters (heart rate and mean arterial blood pressure) of resting unanesthetized adult male Sprague-Dawley rats exposed to a 1.0 mW/cm^2, 435-MHz pulsed-wave (1.0 μs pulse width, 1-kHz pulse rate) RFR environment. The exposure group consisted of 100 cannulated rats housed in Plexiglas cages arrayed on the tiers of a stacked, parallel-plate circular waveguide. Engineering aspects of this waveguide and the exposure environment it generated have been previously reported [11]. The sham-exposure group consisted of 100 cannulated rats housed in an identical, but unenergized, collocated facility.

II. MATERIALS AND METHODS

Heart rate and mean arterial blood pressure, two stable and sensitive cardiovascular indicators, were chosen to be studied in rats to ascertain whether there were possible environmental stresses induced by chronic RFR exposure. Heart rate and arterial blood pressure were measured in 22 exposed and 22 sham-exposed animals. Any significant increase in the resting heart rate and arterial blood pressure would have been interpreted as effects of long lasting, low-level stress induced by RFR.

Animals. Male Sprague-Dawley rats were used in this study. All experimental animals were obtained from the same building and room at CAMM Research Labs, Wayne, New Jersey. The animals, weighing approximately 60 g, were delivered to Emory University where they were caged singly and given water and food (Purina Rat Chow) ad libitum. Temperature in the animal rooms was maintained at 24 $\pm$ 1 ^{o}C and the photoperiod was 12 hours/12 hours, with the lighted phase occurring between 8 AM and 8 PM.

Experimental Facility. The Georgia Tech Research Institute's Radiofrequency Radiation Facility [11] consisted of 8 collocated rooms on the basement floor of the Baker Building on the main campus. These 8 rooms provided a closed, complete facility for long-term bioeffects studies involving rodents.

Two identical, collocated rooms in the Facility housed the 100 exposure and 100 sham-exposure animals. Each room contained a stack of circular, parallel-plate waveguides fed by a slotted-cylinder antenna system for radiating the animals. The stacks of parallel waveguides consisted of five, 3.6-m (12 ft.) diameter plates that made up 4 sets of circular waveguides. Twenty-five individually housed rats were positioned around the circumference of each waveguide set. The walls of both rooms were lined with anechoic absorbing material to simulate open-field exposure conditions and were shielded with aluminum foil to prevent excessive microwave leakage radiation.

The circular, parallel-plate waveguide assembly provided a 1.0 mW/cm^2 exposure field around the circumference of the plates. The 45.7-cm (18 in.) plate separation distance permitted propagation of a TE_{10} mode wave with horizontal polarization. The power density displayed a cosine-squared dependency between the plates, with the maximum power density occurring midway between each set of plates. This arrangement positioned the electric field

vector parallel to the rat's longitudinal axis, thereby maximizing the coupling between the electric field and the rat.

A slotted-cylinder antenna with the proper diameter, thickness, slot length, and slot width dimensions fed the stack of circular waveguides in a manner that provided an essentially constant electric field intensity in the azimuth plane.

Cages. In addition to providing for the animal's biological and physical needs, cages also had to be designed such that they were RFR transparent at 435 MHz and could withstand repeated washings and dryings. The cages were therefore constructed of clear Plexiglas, which was essentially RFR transparent at 435 MHz. Clear (rather than colored) Plexiglas also permitted visual observation of the rats. Each cage was 22.9-cm (9 in.) long by 12.7-cm (5 in.) wide by 17.8-cm (7 in.) tall. These dimensions complied with dimensions recommended by the National Institutes of Health for long-term housing of rats [12]. The food hopper and water bottle were placed on the distal side of the cage to minimize their interaction with the exposure field. The glass floor rods in the cage were oriented perpendicular to the cage's long axis to induce the rats to preferentially align themselves parallel to the electric field vector. The sipper tubes of the water bottles were made of glass to be nonperturbing in the field. Evaluations of the cages conducted in the circular, parallel-plate waveguide assembly showed field scattering from the Plexiglas and water to be below the range of detection.

The Radiation Facility contained a data acquisition system for storing and processing experimental data, an electronic balance for weighing the rats during the study, and rooms for transmitter operation, blood sampling, cage washing, and materials storage.

Cannulation. To detect and quantitatively evaluate possible increases in heart rate and mean arterial blood pressure, the resting values of these cardiovascular parameters were measured in control, unirradiated animals. Chronically implanted aortic cannulas [13,14] permitted measurement of heart rate and mean arterial blood pressure, using each animal as its own control. Cannulation was a simple, inexpensive technique for remote, stress-free measurements of circulatory parameters in conscious, unrestrained, and resting rats.

We used PE-10 arterial cannulas in this study. Larger PE-50 cannulas were unsuitable because they could develop blood clots if not drained

frequently. Large cannulas require multiple flushing to remain patent, but flushing might induce strokes in the animals. Chronic cannulation of the aorta with a PE-10 cannula was preferable to cannulation of other arterial blood vessels. Cannulation of the abdominal aorta provided long-term functional cannulas, but the cannulation procedure was lengthy (20-30 min) and required opening the abdominal cavity and temporary dislocation of the gastro-intestinal system. The abdominal aortic cannula had a much larger dead space than the aortic cannula. Cannulation of the aorta through the left carotid artery, on the other hand, required an incision of 1-1.5 cm (0.4-0.6 in.) that neither penetrated body walls nor entered the abdominal cavity. Further, this cannulation could be completed in approximately 8 min.

The carotid artery of the animal was cannulated 8 to 10 days before the animals entered the study. The surgery was done using ketamine-xylazine anesthesia (1:1 mixture; ketamine 100 mg/mL, xylazine 20 mg/mL, i.m. 0.1 mL/100 g of body weight). The cannula was filled with slightly heparinized saline* and the distal end was sealed with a nylon plug. The first cardiovascular measurements occurred once the animals completely recovered from surgery, normally 10 days after aortic cannulation.

Circulatory Measurements. Restraint and handling increase heart rate and arterial blood pressure in rats (Fig. 1). However, the animals had to be handled upon removal from their RFR exposure cage and placed in the "sampling box" in preparation for heart rate and mean arterial blood pressure measurements. Circulation parameters were measured 30 min after the animal was placed in the sampling box. This procedure gave sufficient time for circulatory parameters to return to their resting values. Each animal was also preconditioned for exposure to the sampling box through a regime of several 30-min-long placements in the box during a 2-week period before entering the study.

After acclimating for 30 min in the sampling box, the rat's cannula was positioned through the slot in the top of the box (Fig. 2) and connected to a Statham transducer. Transducer output was recorded on a Dynagraph strip-chart recorder. Each arterial blood pressure measurement lasted 3 to 5 min. The arterial blood pressure recording was used to count heart rate/minute values. After the recording was finished, the cannula was separated from the Statham transducer and sealed with the nylon plug.

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*0.3-cm³ heparin sodium (from beef lung), 1000 units/mL per 30 cm³ saline.

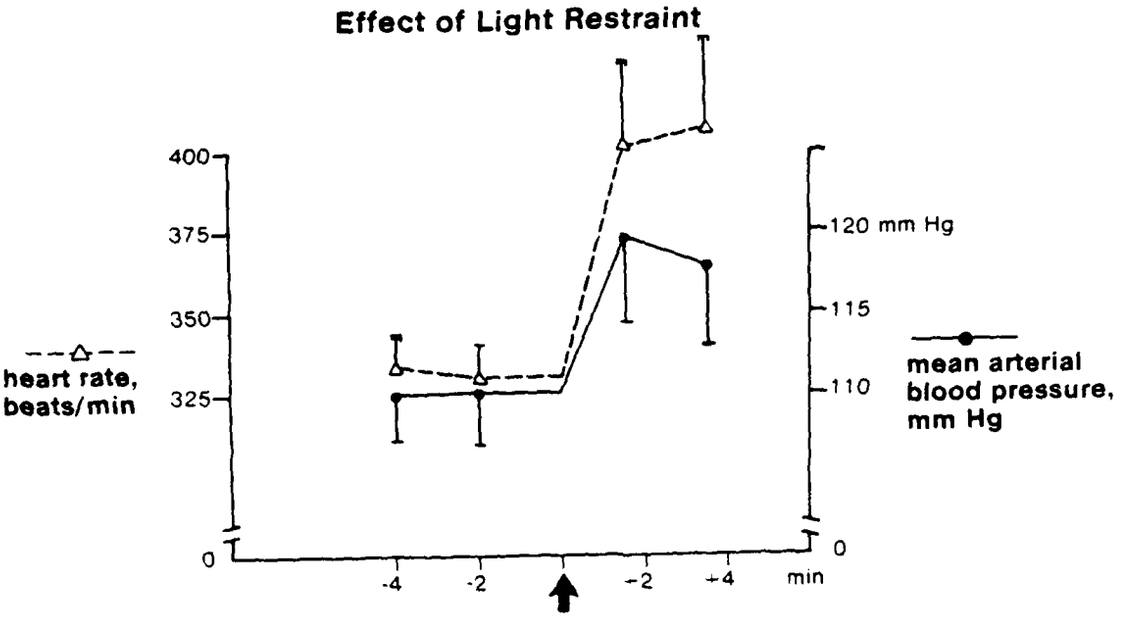

Figure 1. Effect of light restraint on heart rate (beats/min + SD) and mean arterial blood pressure (mm Hg - SD). Rats were placed in a narrow box at arrow (N = 6).

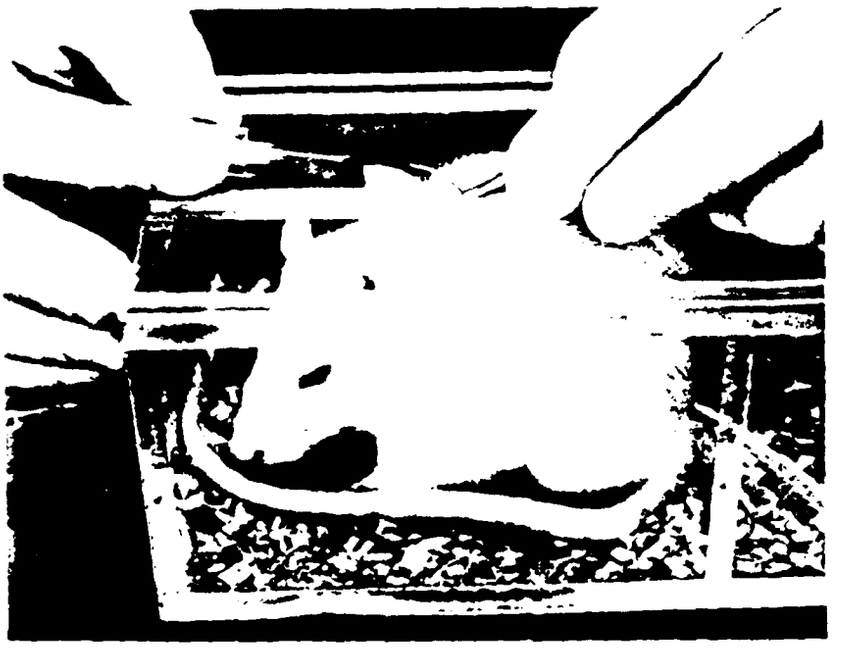

Figure 2. Chronically cannulated rat in sampling box.

Anesthesia was not used during circulatory measurements because anesthetic agents decrease heart rate and arterial blood pressure (Fig. 3) [15]. Since heart rate and arterial blood pressure follow a circadian rhythm in the rat, the circulatory parameters were collected only between 9 AM and 1 PM.

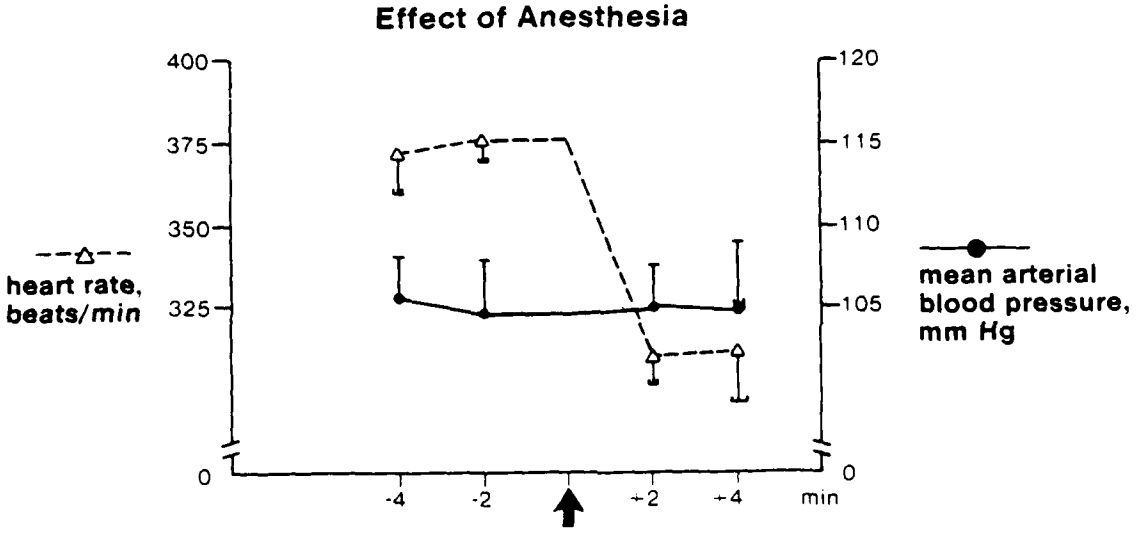

Figure 3. Effect of anesthesia (35 mg/kg of Nembutal) on heart rate (beats/min ± SD) and mean arterial blood pressure (mm Hg ± SD). Nembutal was administered at the arrow.

III. RESULTS AND ANALYSIS

Overview. For a more detailed treatment of the methods used to obtain the heart rate and mean arterial blood pressure analyses, consult the appendixes. A description of the statistical model and application of that model to the heart rate and mean arterial blood pressure data is given in Appendix A. Raw data and pertinent Statistical Analysis System (SAS) regression outputs (such as programs, model-building procedures, lack-of-fit tests, and residual plots) for the heart rate analysis follow in Appendixes B-F; corresponding data and files pertaining to the mean arterial blood pressure analysis follow in Appendixes G-K.

Heart Rate. Appendix B contains data collected during the pretreatment and treatment periods for both exposure and sham-exposure groups. Since the data were directly collected in the Radiation Facility (rather than obtained after a hormone assay), there was less variance present in this data set when compared to data sets obtained from hormone assays (see [8,9,10]). Also, since all the values were directly read in the Radiation Facility, there was a chance to monitor and correct erroneous observations (such as ones due to improper calibration of equipment), thereby eliminating outliers from the data set (i.e., there was no way of obtaining an "absolutely wrong" value of heart rate--say, one in the thousands--without knowing it and repeating the measurement until the true value was obtained).

Figures 4 and 5 show the heart rate data as a scatter diagram. The dotted lines pass through the mean heart rate at each week data were collected. The mean heart rate of the exposure group did not appear to differ from that of the sham-exposure group (Fig. 6), indicating that chronic exposure to 435-MHz RFR did not alter resting heart rate in the rats. To attach a numerical probability to this conclusion, a statistical analysis was performed on the data.

Using multiple linear regression procedures, a quadratic model was built to describe animal heart rate as a function of incident RFR and time. Terms of this model were then tested for their significance in describing the heart rate data set.

The statistical analysis indicated that neither RFR nor time had any effects on heart rate in either the exposure or sham-exposure groups. The pooled mean (over the entire study) was calculated to be 374 beats/min in the sham-exposure animals (n = 127) and 373.3 beats/min in the exposure animals (n =

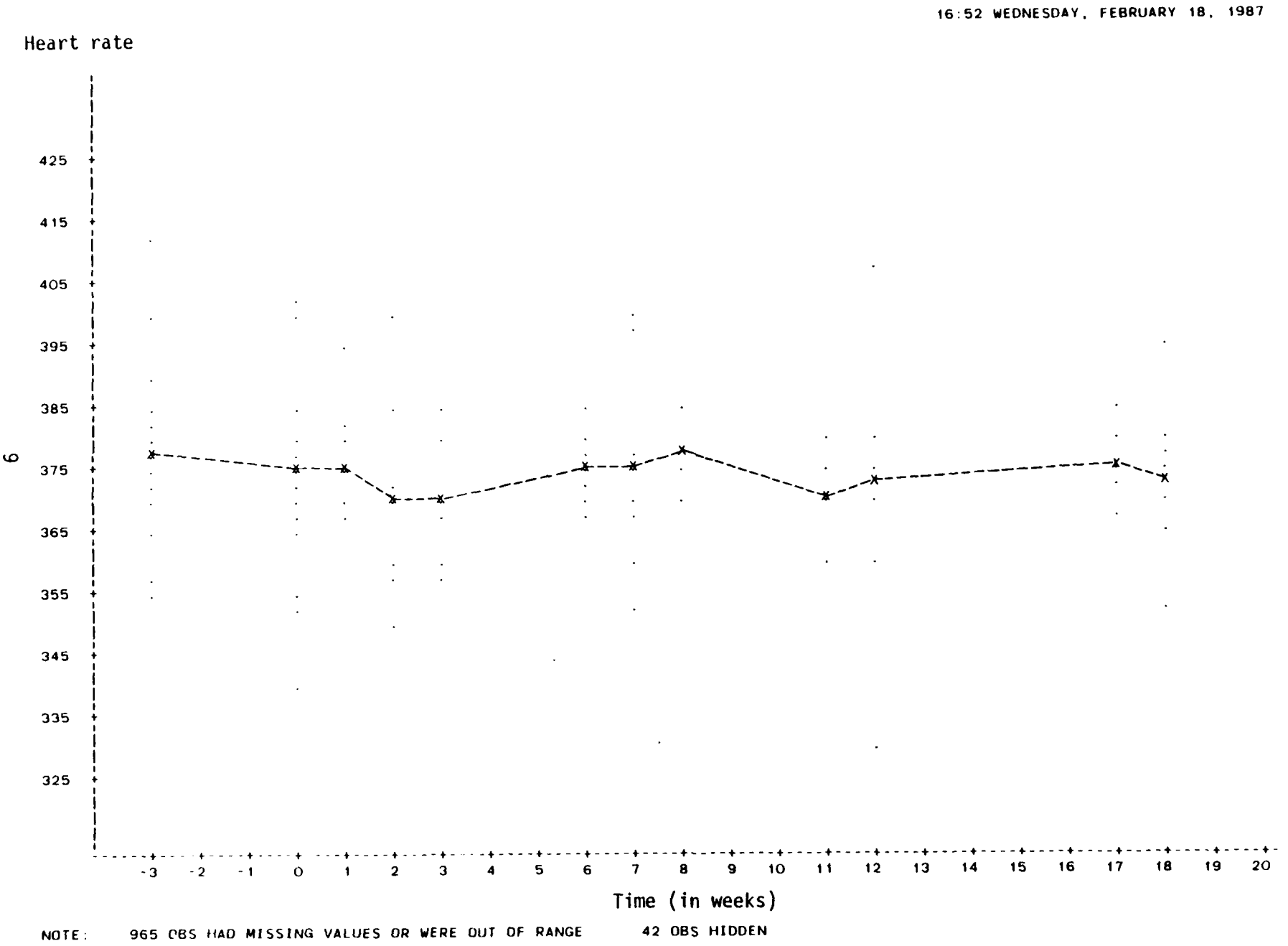

Figure 4. Heart rate data scatter diagram (sham-exposure group).

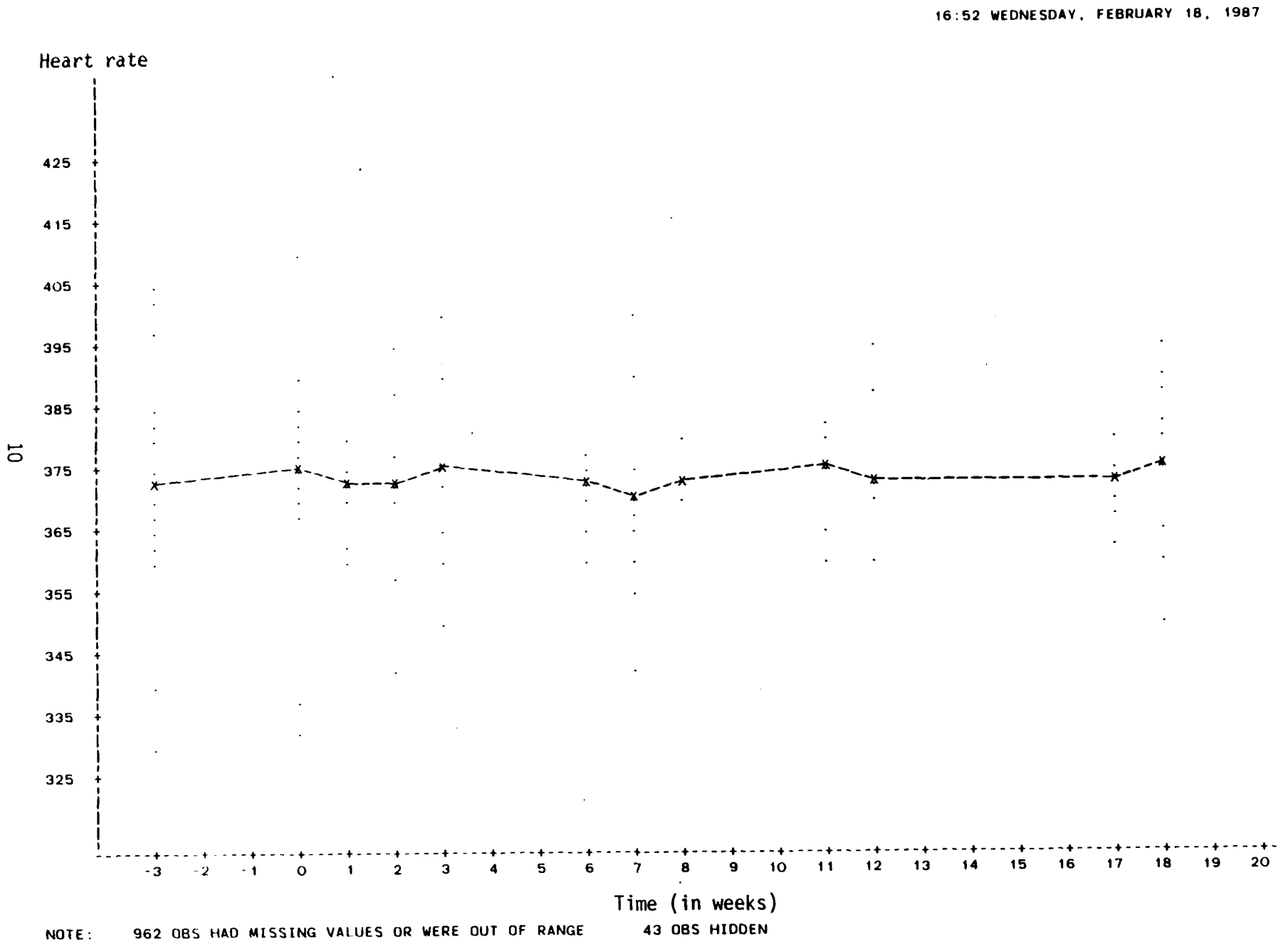

Figure 5. Heart rate data scatter diagram (exposure group).

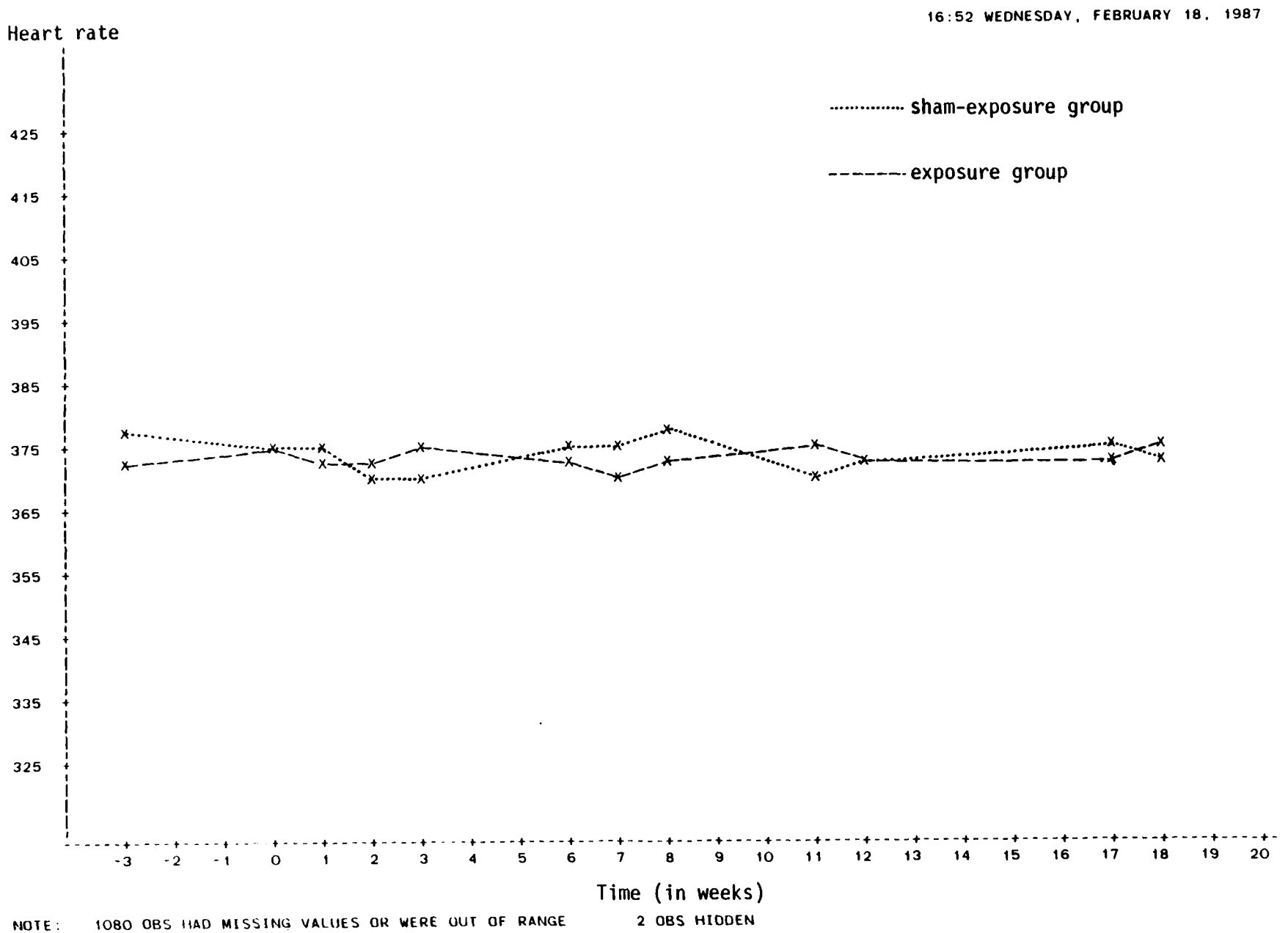

Figure 6. Mean heart rate versus time.

129). This result was not altogether surprising. Previous analyses did not show any significant hormonal increases (ACTH, corticosterone, prolactin, norepinephrine, epinephrine, and dopamine) resulting from the 435-MHz RFR environment. RFR-induced increases in the plasma concentrations of these hormones would probably have affected heart rate.

Further analysis indicated that, if RFR induced a difference of 5 beats/min between the 2 groups, the protocol would have detected the change at a 90% probability. A 5 heartbeat/min difference from the estimated resting heartbeat of 373.7 would yield a range of 368 to 388 beats/min. These values are well within established boundaries for unstressed, healthy male Sprague-Dawley rats (260 to 450 beats/min). Therefore, chronic exposure to the 435-MHz RFR environment did not appear to have affected the animal resting heart rates.

Mean Arterial Blood Pressure. Appendix G contains the data collected during the pretreatment and treatment periods for both exposure and sham-exposure animals. Like the heart rate data, these data were collected in the Radiation Facility, and therefore have a smaller variance than the assay data.

Figures 7 and 8 present the mean arterial blood pressure data as scatter diagrams. Once again, the dotted lines pass through the mean arterial blood pressure at each week data were collected. The mean arterial blood pressure of animals in the exposure group did not appear to differ from that of animals in the sham-exposure group (Fig. 9). To confirm this hypothesis, a statistical analysis similar to that performed on the heart rate data was also applied to the mean arterial blood pressure data.

The statistical analysis indicated that neither RFR nor time had any effect on the resting mean arterial blood pressure (112 mm Hg). The pooled mean (over the entire study) was calculated to be 112.2 mm Hg in the sham-exposure animals (n = 128) and 111.6 mm Hg in the exposure animals (n = 129). This result complements that observed in the heart rate analysis.

Further analysis indicated that if RFR induced a difference of 2.6 mm Hg between the 2 groups, the protocol would have detected the change at a 90% probability. Blood pressures within the range of 109 to 115 mm Hg are typical of unstressed, healthy male Sprague-Dawley rats. Thus, chronic exposure to the 435-MHz RFR environment did not change the animal's mean arterial blood pressure.

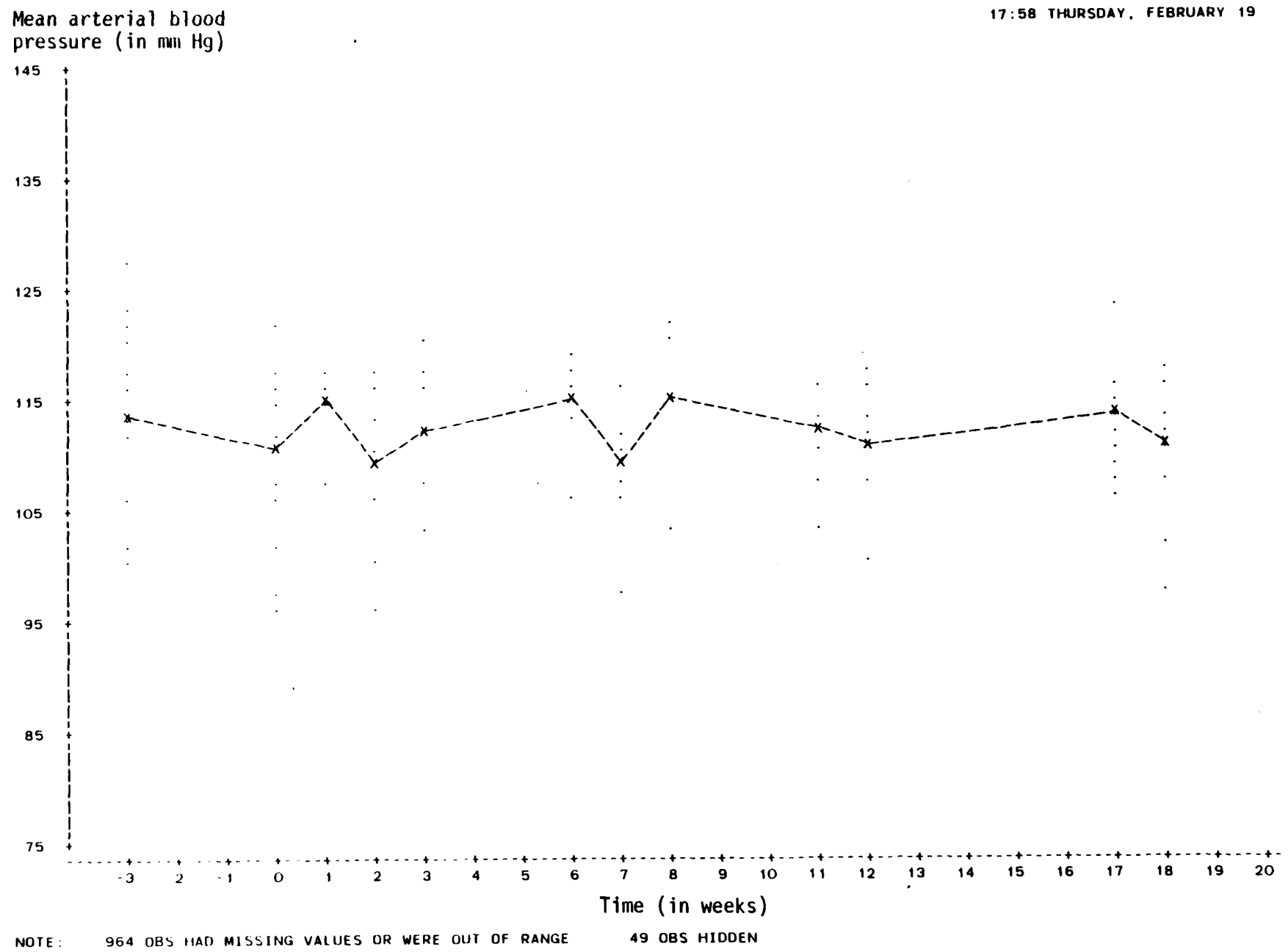

Figure 7. Mean arterial blood pressure data scatter diagram (sham-exposure group).

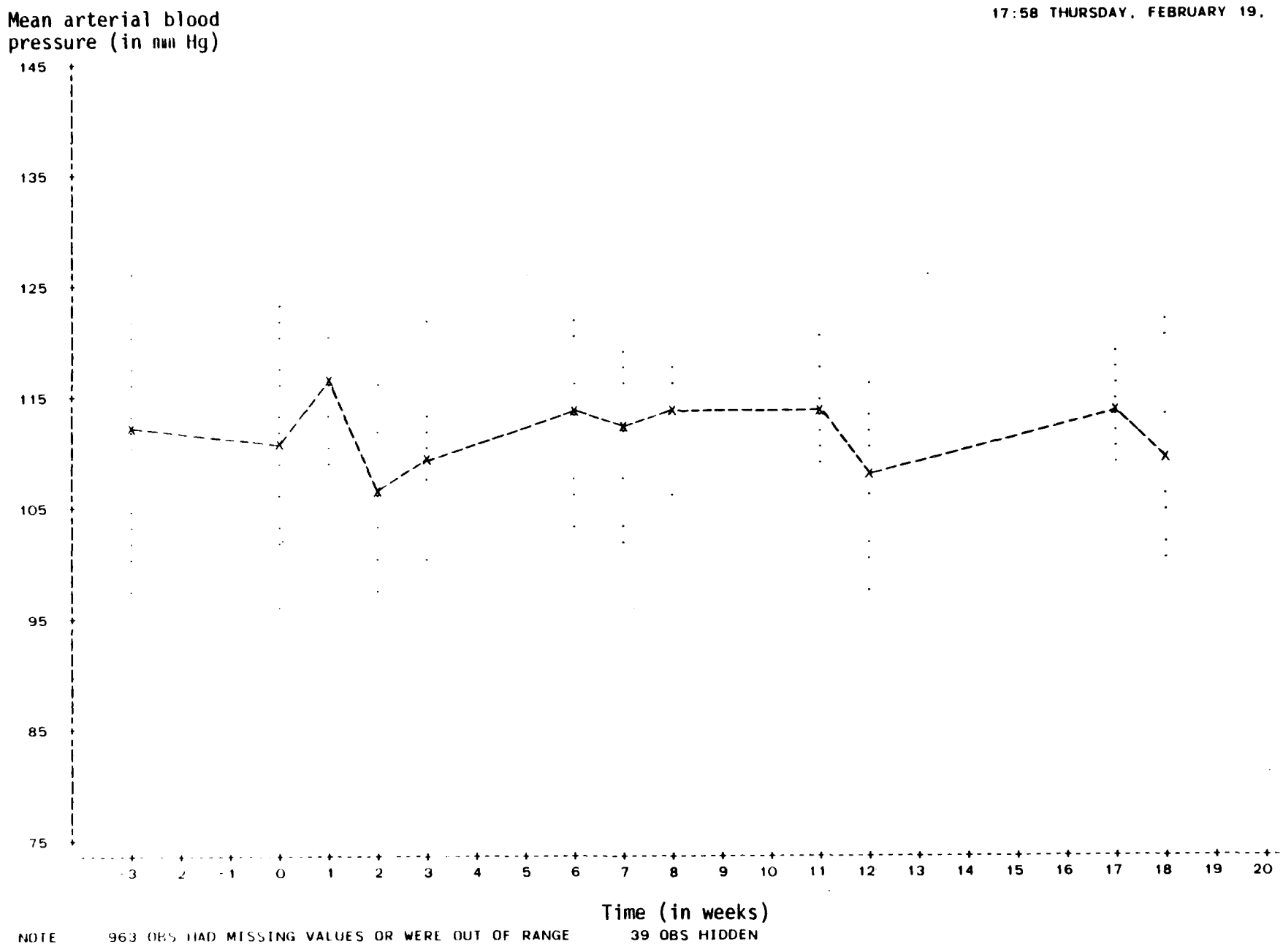

Figure 8. Mean arterial blood pressure data scatter diagram (exposure group).

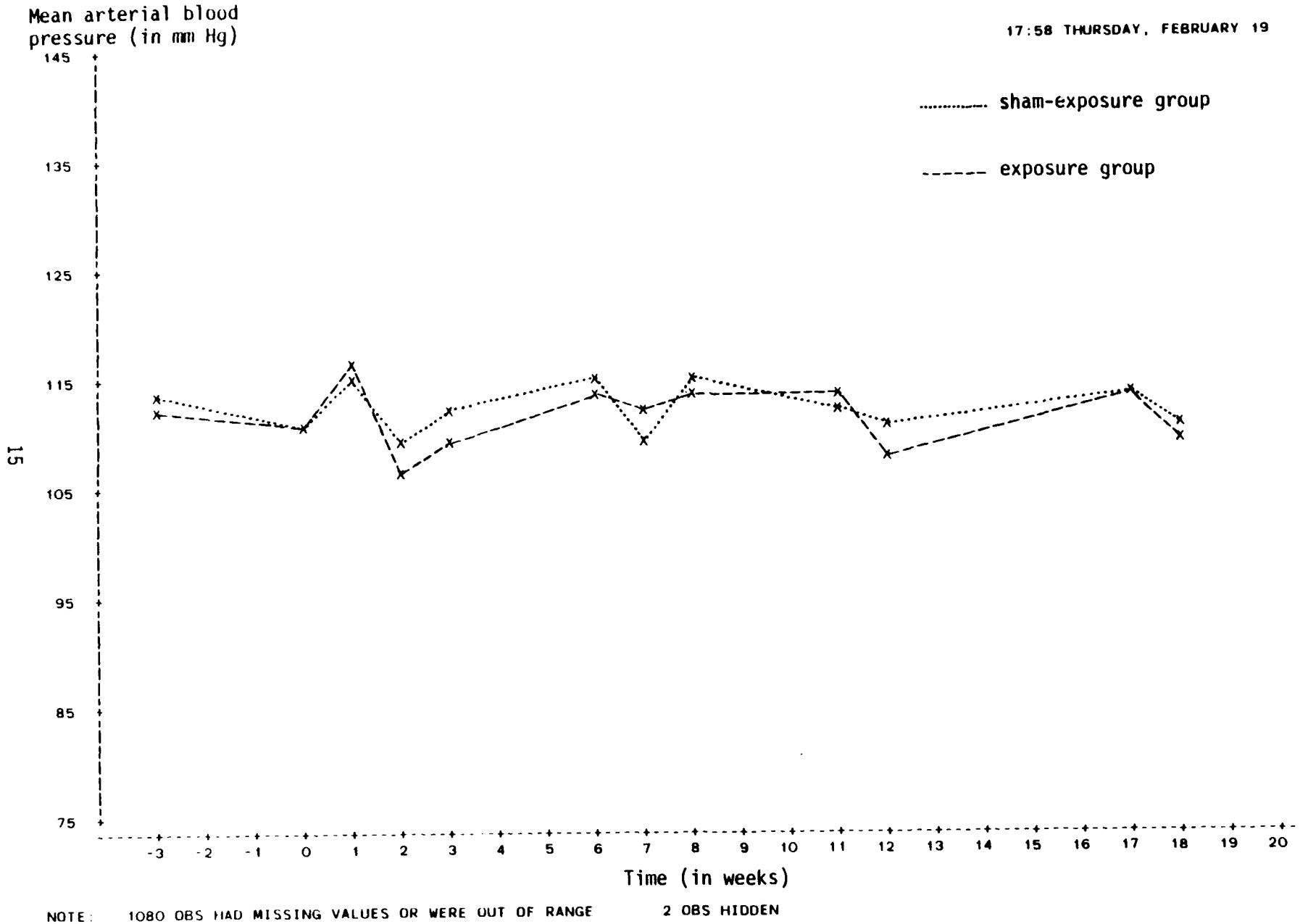

Figure 9. Mean arterial blood pressure versus time.

IV. DISCUSSION

One of the known effects of RFR exposure is on circulation. Changes observed include hypotonus, bradycardia, delayed atrial and ventricular conduction, decreased arterial blood pressure, and electrocardiographic alterations. Michaelson noted that circulatory changes do not diminish work capacity, and are reversible [16]. Sometimes the circulation changes are so small that they are hardly detectable. Small increases in temperature brought on by radiation might induce profound changes in circulation; similar circulatory changes are observed when body temperature is increased during exercise or external heat exposure.

There are several reports that acute microwave radiation has a chronotropic heart response both in vivo or in vitro. Presman and Levitina [17], and Levitina [18] reported chronotropic effects in rabbits after exposure to continuous-wave (CW) microwave fields (wavelength = 12.5 cm (5 in.)) of 5 and 10 mW/cm^2 incident power. Depending on direction of the field (dorsal or ventral), they observed bradycardia or tachycardia. It is important to note that the rabbits in these experiments were immobilized and immobilization is a stress that by itself releases catecholamines and thus increases heart rate. Other Russian works [19,20] also describe microwave effects on heart rate, arterial blood pressure, and other cardiovascular parameters. More recently, Lu et al. [21] found heart rate changes in dogs whose heads were radiated, while Olson et al. [2] saw bradycardia in isolated rat hearts during microwave exposure. Galvin et al. [22] described the effect of RFR on spontaneously beating rat atria. In anesthetized rats exposed to 60 mW/cm^2 of 5.6 GHz RFR (hyperthermia of 1 ^{o}C), Jauchem et al. [23] saw tachycardia, but not when this field intensity was decreased by 50%. These studies indicate that heart rate changes are related to average power density. Galvin and McRee [3] acutely exposed (for 6 h) rats to 2450 MHz microwave radiation at a specific absorption rate (SAR) of 3.7 mW/g. After 1 hour of the exposure and during the following 5 hours, the heart rate of the radiated rats decreased from 450 to 400 beats/min while mean arterial blood pressure remained unchanged at 120 $\pm$ 5 mm Hg. The investigators attributed heart rate decrease to a reduction of the resting metabolic rate induced by microwave heating. But, Kaplan et al. [4], and Chou et al. [5] did not see chronotropic effects of microwaves on the heart rate in adult animals. Hamrick and McRee [24] exposed 9- to 13-day-old quail embryos to 2.45-GHz

microwave radiation at SARs of 0.3 to 30 mW/g. No effects on heart rate were noted. Similarly, Liu et al. [25] did not find changes in the rates of frog hearts irradiated in situ.

In our experiments low-level RFR exposure lasting several months did not change the heart rate or mean arterial blood pressure of resting, unanesthetized rats temporarily removed from the RFR field. These results support an earlier finding obtained in the same animals: low-level RFR exposure lasting 5 months did not change resting plasma norepinephrine and epinephrine concentrations of the rats. Catecholamines have a direct effect on heart rate, as well as on the mean arterial blood pressure; small increases in plasma catecholamines lead to increases of both circulatory parameters.

It has been reported further that young subjects have a lower mean arterial blood pressure than old subjects and at the same time a lower circulating level of norepinephrine [26]. In our experiment we did not observe changes in the arterial blood pressure (or in plasma norepinephrine level), either in exposed or control animals, over a period of 6 months. We have observed unchanged heart rate and mean arterial blood pressure in rats over even longer periods of time [15].

As mentioned before, our earlier work (unchanged resting level of plasma norepinephrine and plasma epinephrine in rats) [8] and the present work (unchanged heart rate and unchanged mean arterial blood pressure) suggest a study to measure cardiac output during RFR exposure. Chronic aortic and right ventricular cannulas in the rats would permit measurement of cardiac output, O_2 consumption, and Fick principle without using standard implantable metal blood flow probes. Knowledge of cardiac output would provide a proper description of cardiovascular status during RFR exposure.

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APPENDIX A

STATISTICAL METHODOLOGY

APPENDIX A

STATISTICAL METHODOLOGY

Originally, data from this experiment was to be analyzed using a 2-way, fixed effects analysis of variance (ANOVA). The 2 treatments were RFR, with 2 levels (corresponding to exposure and sham-exposure), and time, with 12 levels (corresponding to the number of times heart rate and arterial blood pressure were required to be measured in the protocol). The ANOVA would then be able to detect changes in the normal resting value as induced by RFR, time, or the interaction between RFR and time.

However, data collection did not proceed according to protocol. In numerous cases, observations were collected at odd intervals (invalidating design orthogonality), or the number of observations taken per week varied (invalidating design balance). Both of these problems will lower the power of an ANOVA test, making it more difficult to detect effects on the normal resting value.

Data of this type has been treated successfully in the past by employing linear regression techniques to develop, build, and test a linear (or intrinsically linear) model whose parameters can be used to predict system response at various treatment levels. In this experiment, a particularly useful model to test for the presence of RFR-induced effects, and the model used in the ACTH/corticosterone, prolactin, and catecholamine analyses, was:

$$y = \beta_0 + \beta_1 x + \beta_{11} x^2 + \alpha_0 z + \alpha_1 zx + \alpha_{11} zx^2 \qquad \text{(A-1)}$$

where y = animal response (either heart rate or mean arterial blood pressure),

x = time (in weeks), and

z = a categorical variable with value 0 for animals in the sham-exposure group and value 1 for animals in the exposure group.

The parameters β_1, β_{11}, α_0, α_1, and α_{11} all tested for various time-related or RFR-related effects. Specifically, the hypothesis each term tested was as follows:

H_0: $\beta_1 = 0$ (A-2)

H_1: $\beta_1 \neq 0$ (time effected animal response in a linear manner throughout the study),

H_0: $\beta_{11} = 0$ (A-3)

H_1: $\beta_{11} \neq 0$ (the animal displayed some curvature in response throughout the study),

H_0: $\alpha_0 = 0$ (A-4)

H_1: $\alpha_0 \neq 0$ (RFR biased the resting value of the response at the study initiation),

H_0: $\alpha_1 = 0$ (A-5)

H_1: $\alpha_1 \neq 0$ (RFR biased the resting value in a linear manner throughout the duration of the study), and

H_0: $\alpha_{11} = 0$ (A-6)

H_1: $\alpha_{11} \neq 0$ (RFR induced some curvature in the resting value throughout the duration of the study).

The advantage of the regression approach to data analysis was that it provided a way to use all the study data collected, even though the number of replications per week and the weeks of data collection varied throughout the experiment. A regression model would be able to answer the same questions as the ANOVA (Was there an RFR-induced effect? Did it increase or decrease the group response?), as long as the assumptions used in building the regression model were satisfied.

Heart Rate Statistical Analysis

Data from the heart rate spreadsheets (Appendix B) were put on computer file, and a Statistical Analysis System (SAS) formatting program (Appendix C) was prepared to read the data and perform the desired statistical tests on the model.

The first test identified terms within the model which contributed the least toward forming a statistically significant regression. These procedures were used in combination with an initial regression on the general model (not included) to evaluate the statistical significance of terms modeling the heart

rate time dependency and terms modeling the RFR-induced effects on heart rate. Two types of model "building" procedures were employed: forward stepwise regression and maximum R^2 regression. Forward stepwise regression produced a model by calculating F statistics for all variables not in the model, and then adding a variable to the model if its F statistic was significant at a given risk (for this reason, the forward procedure begins with no variables in the model). Once a variable was added to the model, the procedure recalculated F statistics for all the terms in the model, and rejected any terms whose F statistic rose above a given α risk. In this manner, forward stepwise regression eventually settled on a model including all terms whose α risk was low enough to permit initial entry and then not be rejected upon the addition of other terms.

Maximum R^2 regression took this procedure further, producing lists of the best 1-parameter model, best 2-parameter model, best 3-parameter model, etc., until all the parameters were included in the final model. This procedure permitted choosing different models using number of parameters as a criterion.

Both regression techniques failed to find any statistically significant regressor variables (Appendix D). Therefore, the model indicated by the analysis was the straight line

$$y = \beta_0, \tag{A-7}$$

where $\beta_0 = 373.68$ heartbeats/min.

The entry and exit risk for the procedures were both set at $\alpha = 0.15$. Therefore, there was no difference in heart rate between the exposure group animals and the sham-exposure group animals for the duration of the study. The result confirmed the intuitive hypothesis (arrived at by examining Figure 6 in the RESULTS AND ANALYSIS section of the report) that there were no RFR- or time-dependent effects on animal resting heart rate. The mean (pooled over time) resting heart rate was 374 beats/min in the sham-exposure animals (n = 127); 373.3 beats/min in the exposure animals (n = 129), with sample standard deviations of 12.43 and 13.75 beats/min respectively.

This conclusion could be accepted upon verification of the few assumptions used in forming the model. Model lack-of-fit tests (Appendix E) gave an indication of how precise the straight-line model fit the data. Since the F

value obtained from the lack-of-fit test fell below 1.0, there was no indication of any significant model lack-of-fit. Plots of residuals and studentized residuals versus time and animal ID number were generated and evaluated. The lack of a regression in the final heart rate model implied that the model predicted a single value of heart rate over the experimental duration for both exposure and sham-exposure groups. Thus, there was no reason to produce a plot of residuals versus predicted value of heart rate. Examination of the heart rate residual plots (Appendix F) showed no skewed or abnormal patterns. Since there was no regression between heart rate and time or heart rate and RFR, there was no need to perform an autocorrelation on the heart rate data.

The assumptions used to produce the model of heart rate versus time and RFR were not violated. Therefore, the empirical model (and conclusions that are provided) can be considered to be both accurate and reliable.

To arrive at a conservative estimate of the minimum change due to RFR in resting animal heart rate which this protocol was capable of detecting, the value of the 2-way analysis of variance operating curve parameter Φ corresponding to the RFR factor (briefly discussed at the beginning of this section) was calculated. This parameter was given by

$$\Phi^2 = \frac{naD^2}{2b\sigma^2} , \qquad \text{(A-8)}$$

where n = number of replications per cell = 20,

a = number of levels in time treatment = 8 (ideally should have been 12),

b = number of levels in RFR treatment = 2,

D = detection threshold, and

σ^2 = population variance.

Substituting values for a, b, n and the sample standard deviation (as an estimate of σ^2) yielded:

$$\Phi = 0.4816D. \qquad \text{(A-9)}$$

To obtain a value of Φ from the operating curve, the type I risk α and type II risk β were set to 0.05 and 0.10 respectively. The value of Φ was then read

from the fixed effects ANOVA operating curve with $\nu_1 = 1$ and $\nu_2 = 304$. This value was

$$\Phi = 2.4. \qquad \text{(A-10)}$$

The numerator degrees of freedom (ν_1) and the denominator degrees of freedom (ν_2) were calculated using the equations

$$\nu_1 = b - 1, \text{ and} \qquad \text{(A-11)}$$
$$\nu_2 = ab\ (n - 1). \qquad \text{(A-12)}$$

In this particular experiment, the replications n were not replications in the strictest sense of the word (since a true replication would require taking a single rat and running it through the experiment n times). However, since Sprague-Dawley rats represent a very homogeneous population (particularly when acquired at the same time from the same room and distributor), the inter-animal variation should be minimal.

By substitution, the detection level was therefore

$$D_B = 4.9833 \text{ beats}. \qquad \text{(A-13)}$$

Thus, the protocol should have been able to detect a 5 beat difference between the 2 groups approximately 90% of the time. For comparison purposes, the calculated difference between groups was found to be only 1 beat. This calculation demonstrated why the null hypothesis was not rejected in the analysis.

Mean Arterial Blood Pressure Statistical Analysis

Data from the mean arterial blood pressure spreadsheets (Appendix G) were put on a second computer file, and a new SAS formatting program (Appendix H) was prepared to read the data and perform the desired statistical tests on the model.

As was the case with the heart rate analysis, the first test performed was a stepwise/maximum R^2 set of regressions on the model

$$y = \beta_0 + \beta_1 x + \beta_{11} x^2 + \alpha_0 z + \alpha_1 zx + \alpha_{11} zx^2 \qquad \text{(A-14)}$$

(all variables as defined previously; y = mean arterial blood pressure in mm Hg), to determine the significance of the α terms modeling the RFR effect on mean arterial blood pressure. The two regressions yielded no parameters significant at an entry risk of 0.15 (Appendix I). The final model of mean arterial blood pressure in this study was then the average of all animal blood pressures pooled over both time and exposure/sham-exposure groups:

$$y = 111.9 \text{ mm Hg} \qquad \text{(A-15)}$$

This result indicated no difference between exposure and sham-exposure groups in mean arterial blood pressure. The mean (pooled over time) arterial blood pressure in the sham-exposure group was 112.2 mm Hg (n = 128); in the exposure group, 111.6 mm Hg (n = 129). Thus, it appeared that chronic exposure to 435-MHz RFR (in this 1.0 mW/cm^2, 1-kHz pulse rate environment) had no effect on the mean arterial blood pressure of the exposure group, when compared to the sham-exposure group.

The first test performed to verify the mean arterial blood pressure model was to check the model for lack-of-fit (Appendix J). The computed F statistic of 1.26 was slightly larger than the critical F value (α of 0.10) of 1.22; thus indicating a slight degree of lack-of-fit. However, the value of the test statistic and critical value are so close that one can still consider model fit to be satisfactory. The relatively high value of the test statistic (when compared to its counterpart calculated in the heart rate analysis) is a measure of the greater "spikiness" found in the graph of mean arterial blood pressure versus time.

Examination of the residual plots in Appendix K (residuals and studentized residuals versus time and animal ID number) also yielded no significant patterns within the data. The residuals were thus distributed normally with mean zero and variance σ^2.

The final step was to determine the minimum change due to RFR that the protocol was capable of reliably detecting. The equations are identical to those used in the preceding heart rate analysis, with the only difference being the value of the sample standard deviation substituted into the equation.

Therefore,

$$\Phi_B^2 = \frac{naD^2}{2b\sigma^2} \quad ; \quad \Phi = 0.9361D. \tag{A-16}$$

The value of Φ_B from the ANOVA operating curve is the same as that found in the heart rate analysis. Therefore, the detection threshold D was

$$D = 2.56 \text{ mm Hg}. \tag{A-17}$$

The protocol would have detected a 2.6 mm Hg difference between the exposure and sham-exposure groups approximately 90% of the time. For comparison purposes, the calculated difference in mean arterial blood pressure between the 2 groups was under 1 mm Hg. This calculation demonstrated why the null hypothesis was not rejected in the analysis.

We gratefully acknowledge the assistance of Dr. Russell G. Heikes of Georgia Tech's Department of Industrial and Systems Engineering in developing the statistical methodology of this Appendix.

APPENDIX B

RAW HEART RATE DATA SPREADSHEETS

Heart Rate (Controls I)

Rat #	Group	-3WK	-2WK	0WK	TIME 1WK	2WK	3WK	4WK	5WK	6WK	7WK	8WK	9WK	10WK	11WK	12WK	13WK	14WK	15WK	16WK	17WK	18WK	19WK	20WK
1		372		376	370		380			[illegible]		385			360						368			
2		382		401		369					371					254								
3		376		372	368					376					370						[illegible]	374		
4		391		353		372					377											371		
5		386		380	[illegible]					380					[illegible]	376					386			
6		365		368			358				349											371		
7		380		340	[illegible]		386			375					376						[illegible]	378		
8		354		374		401						376									385			
9		364		364	369					369					[illegible]	376					368			
10		400		402			370				352											364		
11		370		368	[illegible]	360				370					370						368			
12		384		—		358						370				381						390		
13		376		370	375		[illegible]			[illegible]	374				370						374			

Heart Rate (Controls II)

Rat #	Group	-3WK	-2WK	0WK	TIME 1WK	2WK	3WK	4WK	5WK	6WK	7WK	8WK	9WK	10WK	11WK	12WK	13WK	14WK	15WK	16WK	17WK	18WK	19WK	20WK
14		375		370	376					372					370						368			
15		412		372			371				370					370						394		
16		[illegible]		378	380					378					370						375			
17		355		375		373					[illegible]					—						370		
18		360		370	370					370					375						373			
19		378		355			361				348					407						370		
20		350		372	382					369					369						373			
21		357		403		350					359					330						352		
22		339		[illegible]	[illegible]	325				355					330						330			
23																								
24																								
25																								
26				-																				

Heart Rate (Microwaves I)

Rat #	Group	-3WK	-2WK	0WK	TIME 1WK	2WK	3WK	4WK	5WK	6WK	7WK	8WK	9WK	10WK	11WK	12WK	13WK	14WK	15WK	16WK	17WK	18WK	19WK	20WK
1		375		373	376		390			[illegible]		369			374						375			
2		382		411		358					361					373								
3		380		383	376					376					382						380	380		
4		362		337		370					354											364		
5		362		368	360					360					[illegible]	372					368			
6		405		368			392				390											388		
7		370		370	364		364			372					376						376	376		
8		331		391		378						370									379			
9		384		376	374					375					[illegible]	370					376			
10		360		370			400				369											390		
11		370		378	388	388				370					376						380			
12		402		411		342						380				360						359		
13		374		374	363		372			[illegible]	374				376						376			

Heart Rate (Microwaves II)

Rat #	Group	-3WK	-2WK	0WK	TIME 1WK	2WK	3WK	4WK	5WK	6WK	7WK	8WK	9WK	10WK	11WK	12WK	13WK	14WK	15WK	16WK	17WK	18WK	19WK	20WK
14		376		381	381					372	[illegible]				380						376			
15		341		377			360				364					361						350		
16		370		378	372					366					365						368			
17		374		332		372					342					[illegible]						396		
18		362		384	376					376					380						362			
19		398		372			351				400					394						383		
20		364		372	370					378					360						374			
21		368		384		396					368					370						375		
22		376		382	[illegible]	371				371					374						378			
23																								
24																								
25																								
26																								

APPENDIX C

HEART RATE SAS FORMATTING PROGRAM

```
1          SAS(R) LOG  CMS SAS 5.16       VM/CMS CMS USER QSECLSB

NOTE: COPYRIGHT (C) 1984,1986 SAS INSTITUTE INC., CARY, N.C.  27511, U.S.A.
NOTE: CMS SAS RELEASE 5.16 AT GEORGIA INSTITUTE OF TECHNOLOGY (03559001).

NOTE: CPUID   VERSION = FF  SERIAL = 012242  MODEL = 4381 .

NOTE: SAS OPTIONS SPECIFIED ARE:
      LEAVE=0

  1 DATA TESTH;
  2 CMS FILEDEF X DISK HEARTRT DAT A;
  3 CMS FILEDEF 20 DISK HEARTRT0 LISTING A1 ( BLKSIZE 141 RECFM VBA LRECL 133;
  4 CMS FILEDEF 21 DISK HEARTRT1 LISTING A1 ( BLKSIZE 141 RECFM VBA LRECL 133;
  5 CMS FILEDEF 22 DISK HEARTRT2 LISTING A1 ( BLKSIZE 141 RECFM VBA LRECL 133;
  6 CMS FILEDEF 23 DISK HEARTRT3 LISTING A1 ( BLKSIZE 141 RECFM VBA LRECL 133;
  7 CMS FILEDEF 24 DISK HEARTRT4 LISTING A1 ( BLKSIZE 141 RECFM VBA LRECL 133;
  8 CMS FILEDEF 25 DISK HEARTRT5 LISTING A1 ( BLKSIZE 141 RECFM VBA LRECL 133;
  9 CMS FILEDEF 26 DISK HEARTRT6 LISTING A1 ( BLKSIZE 141 RECFM VBA LRECL 133;
 10 CMS FILEDEF 27 DISK HEARTRT7 LISTING A1 ( BLKSIZE 141 RECFM VBA LRECL 133;
 11 ARRAY WEEK {24} WKN3 WKN2 MISSN1 WK0-WK20;
 12 KEEP X XSQR Y Z XZ XSQRZ CASE;
 13 INFILE X;
 14 INPUT CASE 1-3
 15       WKN3 5-7
 16       WKN2 9-11
 17       WK0 13-15
 18       WK1 17-19
 19       WK2 21-23
 20       WK3 25-27
 21       WK4 29-31
 22       WK5 33-35
 23       WK6 37-39
 24       WK7 41-43
 25       WK8 45-47
 26       WK9 49-51
 27       WK10 53-55
 28       WK11 57-59
 29       WK12 61-63
 30       WK13 65-67
 31       WK14 69-71
 32       WK15 73-75
 33       WK16 77-79
 34       WK17 81-83
 35       WK18 85-87
 36       WK19 89-91
 37       WK20 93-95
 38 ;
 39 MISSN1=.;
 40 IF CASE < 100 THEN Z = 0;
 41 IF CASE >= 100 THEN Z = 1;
 42 IF Z=1 THEN CASE=CASE-100;
 43 DO I = 1 TO 24;
 44 X = I-4; XSQR = X*X; XZ = X*Z; XSQRZ = X*X*Z; Y = WEEK {I};OUTPUT;
 45 END;


NOTE: INFILE X IS FILE HEARTRT DAT A1
NOTE: 44 LINES WERE READ FROM INFILE X.
NOTE: DATA SET WORK.TESTH HAS 1056 OBSERVATIONS AND 7 VARIABLES.
```

```
2          SAS(R) LOG  CMS SAS 5.16      VM/CMS CMS USER QSECLSB

NOTE: THE DATA STATEMENT USED 0.34 SECONDS AND 288K.

 46 PROC CONTENTS;
NOTE: THE PROCEDURE CONTENTS USED 0.18 SECONDS AND 544K AND PRINTED PAGES 1 TO 2.

 47 PROC PRINTTO NEW UNIT=20;

NOTE: THE PROCEDURE PRINTTO USED 0.02 SECONDS AND 480K.

 48 PROC SORT OUT=SCTR;
 49       BY Z X Y;

NOTE: DATA SET WORK.SCTR HAS 1056 OBSERVATIONS AND 7 VARIABLES.
NOTE: THE PROCEDURE SORT USED 0.31 SECONDS AND 6944K.

 50 PROC SUMMARY;
 51       BY Z X;
 52       VAR Y;
 53       OUTPUT OUT=OVLMN MEAN=MEAN;
NOTE: THE DATA SET WORK.OVLMN HAS 48 OBSERVATIONS AND 5 VARIABLES.
NOTE: THE PROCEDURE SUMMARY USED 0.32 SECONDS AND 544K.

 54 DATA SHEARTRT;
 55       SET SCTR OVLMN;
 56       BY Z;

NOTE: DATA SET WORK.SHEARTRT HAS 1104 OBSERVATIONS AND 10 VARIABLES.
NOTE: THE DATA STATEMENT USED 0.27 SECONDS AND 480K.

 57 PROC PLOT NOLEGEND DATA=SHEARTRT;
 58       BY Z;
 59       PLOT MEAN*X='X' Y*X='.' / VAXIS=325 TO 425 BY 10 OVERLAY;
 60       TITLE 'HEART RATE SCATTER DIAGRAM';
NOTE: THE PROCEDURE PLOT USED 0.56 SECONDS AND 544K AND PRINTED PAGES 3 TO 4.

 61 PROC PRINTTO NEW UNIT=21;

NOTE: THE PROCEDURE PRINTTO USED 0.02 SECONDS AND 480K.

 62 PROC PLOT NOLEGEND DATA=SHEARTRT;
 63       PLOT MEAN*X='X' / VAXIS=325 TO 425 BY 10;
 64       TITLE 'Mean Animal Heart Rate Versus Time';
NOTE: THE PROCEDURE PLOT USED 0.41 SECONDS AND 544K AND PRINTED PAGE 5.

 65 PROC PRINTTO NEW UNIT=22;
 66       TITLE 'ANIMAL HEART RATE ANALYSIS';

NOTE: THE PROCEDURE PRINTTO USED 0.03 SECONDS AND 480K.

 67 PROC DATASETS;
 68
LIST OF MEMBERS BEFORE UPDATE OF DIRECTORY.
NAME     MEMTYPE             OBS  TRACKS PROT
OVLMN    /DATA                48       1
SCTR     /DATA              1056       1
SHEARTRT/DATA               1104       1
TESTH    /DATA              1056       1
 68       DELETE SCTR;
```

```
3          SAS(R) LOG  CMS SAS 5.16      VM/CMS CMS USER QSECLSB

 69       DELETE OVLMN;
 70       DELETE TESTH;
LIST OF MEMBERS AFTER UPDATE OF DIRECTORY.
NAME     MEMTYPE             OBS  TRACKS PROT
SHEARTRT/DATA               1104       1
NOTE: THE PROCEDURE DATASETS USED 0.13 SECONDS AND 544K.

 71 PROC STEPWISE DATA=SHEARTRT;
 72       MODEL Y = X XSQR Z XZ XSQRZ / STEPWISE MAXR;
NOTE: THE PROCEDURE STEPWISE USED 0.33 SECONDS AND 544K AND PRINTED PAGES 6 TO 8.

 73 PROC PRINTTO NEW UNIT=23;

NOTE: THE PROCEDURE PRINTTO USED 0.02 SECONDS AND 480K.

 74 PROC REG;
 75       MODEL Y =  / PARTIAL;
 76       ID CASE;
ERROR: NEGATIVE SUM OF SQUARES REGRESSION ENCOUNTERED. HAVE YOU RESTRICTED THE INTERCEPT PAR
       NON-POSITIVE-DEFINITE CORRELATION OR SSCP MATRIX?
NOTE: ACOV AND SPEC OPTION ONLY VALID WITH RAWDATA
NOTE: THE PROCEDURE REG USED 0.53 SECONDS AND 800K AND PRINTED PAGES 9 TO 10.

 77 PROC PRINTTO NEW UNIT=24;

NOTE: THE PROCEDURE PRINTTO USED 0.02 SECONDS AND 480K.

 78 PROC GLM;
 79       CLASS X Z;
 80       MODEL Y = X Z X*Z;
NOTE: THE PROCEDURE GLM USED 1.43 SECONDS AND 1184K AND PRINTED PAGES 11 TO 12.

 81 PROC PRINTTO NEW UNIT=25;

NOTE: THE PROCEDURE PRINTTO USED 0.02 SECONDS AND 480K.

 82 PROC REG;
 83       MODEL Y =  / R;
 84       ID CASE;
 85       OUTPUT OUT=RHRTRT R=RESID STUDENT=STUDENT;
ERROR: NEGATIVE SUM OF SQUARES REGRESSION ENCOUNTERED. HAVE YOU RESTRICTED THE INTERCEPT PAR
       NON-POSITIVE-DEFINITE CORRELATION OR SSCP MATRIX?
NOTE: ACOV AND SPEC OPTION ONLY VALID WITH RAWDATA
NOTE: THE DATA SET WORK.RHRTRT HAS 1104 OBSERVATIONS AND 12 VARIABLES.
NOTE: THE PROCEDURE REG USED 2.18 SECONDS AND 800K AND PRINTED PAGES 13 TO 36.

 86 PROC PRINTTO NEW UNIT=26;

NOTE: THE PROCEDURE PRINTTO USED 0.02 SECONDS AND 480K.

 87 PROC PLOT DATA=RHRTRT;
 88       PLOT RESID*X='*' / VAXIS=-45 TO 45 BY 5;
 89       PLOT STUDENT*X='*' / VAXIS=-4 TO 4 BY 0.5;
 90       TITLE 'Heart rate residual plots';
NOTE: THE PROCEDURE PLOT USED 0.50 SECONDS AND 544K AND PRINTED PAGES 37 TO 38.

 91 PROC PRINTTO NEW UNIT=27;
```

```
4          SAS(R) LOG  CMS SAS 5.16      VM/CMS CMS USER QSECLSB

NOTE: THE PROCEDURE PRINTTO USED 0.02 SECONDS AND 480K.

 92 PROC PLOT DATA=RHRTRT;
 93      BY Z;
 94      PLOT RESID*CASE='*' / HAXIS=1 TO 22 BY 1 VAXIS=-45 TO 45 BY 5;
 95      PLOT STUDENT*CASE='*' / HAXIS=1 TO 22 BY 1 VAXIS=-4 TO 4 BY 0.5;
 96      TITLE 'Heart rate residual plots';
NOTE: THE PROCEDURE PLOT USED 0.45 SECONDS AND 544K AND PRINTED PAGES 39 TO 42.
NOTE: SAS USED 6944K MEMORY.

ERROR: ERRORS ON PAGES 3.

NOTE: SAS INSTITUTE INC.
      SAS CIRCLE
      PO BOX 8000
      CARY, N.C. 27511-8000
```

APPENDIX D

STEPWISE AND MAXIMUM R^2 REGRESSION PROCEDURES USED TO BUILD HEART RATE MODEL

STEPWISE REGRESSION PROCEDURE FOR DEPENDENT VARIABLE Y

WARNING: 847 OBSERVATIONS DELETED DUE TO MISSING VALUES.

NOTE: SLENTRY AND SLSTAY HAVE BEEN SET TO .15 FOR THE STEPWISE TECHNIQUE.

NO VARIABLES MET THE 0.1500 SIGNIFICANCE LEVEL FOR ENTRY INTO THE MODEL.

MAXIMUM R-SQUARE IMPROVEMENT FOR DEPENDENT VARIABLE Y

WARNING: 847 OBSERVATIONS DELETED DUE TO MISSING VALUES.

STEP 1 VARIABLE X ENTERED R SQUARE = 0.00077618 C(P) = -0.09932445

	DF	SUM OF SQUARES	MEAN SQUARE	F	PROB>F
REGRESSION	1	34.16385502	34.16385502	0.20	0.6567
ERROR	255	43981.36143681	172.47592720		
TOTAL	256	44015.52529183			

	B VALUE	STD ERROR	TYPE II SS	F	PROB>F
INTERCEPT	373.98876971				
X	-0.05203830	0.11692407	34.16385502	0.20	0.6567

BOUNDS ON CONDITION NUMBER: 1, 1

THE ABOVE MODEL IS THE BEST 1 VARIABLE MODEL FOUND.

STEP 2 VARIABLE XSQR ENTERED R SQUARE = 0.00450434 C(P) = 0.95708817

	DF	SUM OF SQUARES	MEAN SQUARE	F	PROB>F
REGRESSION	2	198.26091693	99.13045846	0.57	0.5636
ERROR	254	43817.26437490	172.50891486		
TOTAL	256	44015.52529183			

	B VALUE	STD ERROR	TYPE II SS	F	PROB>F
INTERCEPT	374.00450402				
X	-0.33614325	0.31389023	197.83573788	1.15	0.2852
XSQR	0.01946710	0.01995982	164.09706190	0.95	0.3303

BOUNDS ON CONDITION NUMBER: 7.205509, 28.82204

THE ABOVE MODEL IS THE BEST 2 VARIABLE MODEL FOUND.

STEP 3 VARIABLE Z ENTERED R SQUARE = 0.00516889 C(P) = 2.78889303

	DF	SUM OF SQUARES	MEAN SQUARE	F	PROB>F
REGRESSION	3	227.51133798	75.83711266	0.44	0.7296
ERROR	253	43788.01395385	173.07515397		
TOTAL	256	44015.52529183			

	B VALUE	STD ERROR	TYPE II SS	F	PROB>F
INTERCEPT	374.34400417				
X	-0.33594499	0.31440533	197.60196574	1.14	0.2863
XSQR	0.01947660	0.01999257	164.25708644	0.95	0.3309
Z	-0.67479213	1.64142601	29.25042105	0.17	0.6813

BOUNDS ON CONDITION NUMBER: 7.205526, 46.23328

MAXIMUM R-SQUARE IMPROVEMENT FOR DEPENDENT VARIABLE Y

THE ABOVE MODEL IS THE BEST 3 VARIABLE MODEL FOUND.

STEP 4 VARIABLE XZ ENTERED R SQUARE = 0.00778013 C(P) = 4.12799454

	DF	SUM OF SQUARES	MEAN SQUARE	F	PROB>F
REGRESSION	4	342.44663898	85.61165974	0.49	0.7402
ERROR	252	43673.07865285	173.30586767		
TOTAL	256	44015.52529183			

	B VALUE	STD ERROR	TYPE II SS	F	PROB>F
INTERCEPT	374.86953665				
X	-0.43206814	0.33602761	286.52849246	1.65	0.1997
XSQR	0.01941520	0.02000603	163.22063683	0.94	0.3327
Z	-1.71830936	2.08322291	117.90833136	0.68	0.4102
XZ	0.19092720	0.23444864	114.93530100	0.66	0.4162

BOUNDS ON CONDITION NUMBER: 8.219725, 78.74797

THE ABOVE MODEL IS THE BEST 4 VARIABLE MODEL FOUND.

STEP 5 VARIABLE XSQRZ ENTERED R SQUARE = 0.00828585 C(P) = 6.00000000

	DF	SUM OF SQUARES	MEAN SQUARE	F	PROB>F
REGRESSION	5	364.70586796	72.94117359	0.42	0.8364
ERROR	251	43650.81942387	173.90764711		
TOTAL	256	44015.52529183			

	B VALUE	STD ERROR	TYPE II SS	F	PROB>F
INTERCEPT	374.87483475				
X	-0.53718798	0.44681076	251.37610772	1.45	0.2304
XSQR	0.02662921	0.02842932	152.58161054	0.88	0.3498
Z	-1.72988473	2.08708742	119.47353895	0.69	0.4080
XZ	0.40019811	0.63032904	70.10259767	0.40	0.5261
XSQRZ	-0.01433995	0.04008222	22.25922899	0.13	0.7208

BOUNDS ON CONDITION NUMBER: 19.11014, 340.6905

THE ABOVE MODEL IS THE BEST 5 VARIABLE MODEL FOUND.

APPENDIX E

HEART RATE LACK-OF-FIT TEST

ANIMAL HEART RATE ANALYSIS 15:52 TUESDAY, APRIL 14, 1987

GENERAL LINEAR MODELS PROCEDURE

DEPENDENT VARIABLE: Y

SOURCE	DF	SUM OF SQUARES	MEAN SQUARE	F VALUE	PR > F	R-SQUARE
MODEL	23	1189.91796860	51.73556385	0.28	0.9996	0.027034
ERROR	233	42825.60732324	183.80088980		ROOT MSE	
CORRECTED TOTAL	256	44015.52529183			13.55731868	

SOURCE	DF	TYPE I SS	F VALUE	PR > F	DF	TYPE III SS	F VALUE
X	11	375.52313406	0.19	0.9982	11	375.65823979	0.19
Z	1	29.65361860	0.16	0.6883	1	12.06232604	0.07
X*Z	11	784.74121594	0.39	0.9599	11	784.74121594	0.39

this term is solely a measure of sum-of-squares pure error.

Partitioning SS_E into SS_{pe} and SS_{lof}

$SS_E = 44015.5259$ $\quad df = 256$

$SS_{pe} = 42825.6073$ $\quad df = 233$

$SS_{lof} = 1189.9186$ $\quad df = 23$

$MS_{lof} = 51.7356$

$MS_{pe} = 183.8009$

$$F_o = \frac{MS_{lof}}{MS_{pe}} = 0.2815$$

∴ model displays insignificant lack-of-fit.

ANIMAL HEART RATE ANALYSIS

ANALYSIS OF VARIANCE

SOURCE	DF	SUM OF SQUARES	MEAN SQUARE	F VALUE	PROB>F
MODEL	0	-3.72529E-09	.	.	.
ERROR	256	44015.52529	171.93565		
C TOTAL	256	44015.52529			

ROOT MSE	.	R-SQUARE	-0.0000
DEP MEAN	373.7043	ADJ R-SQ	-0.0000
C.V.	.		

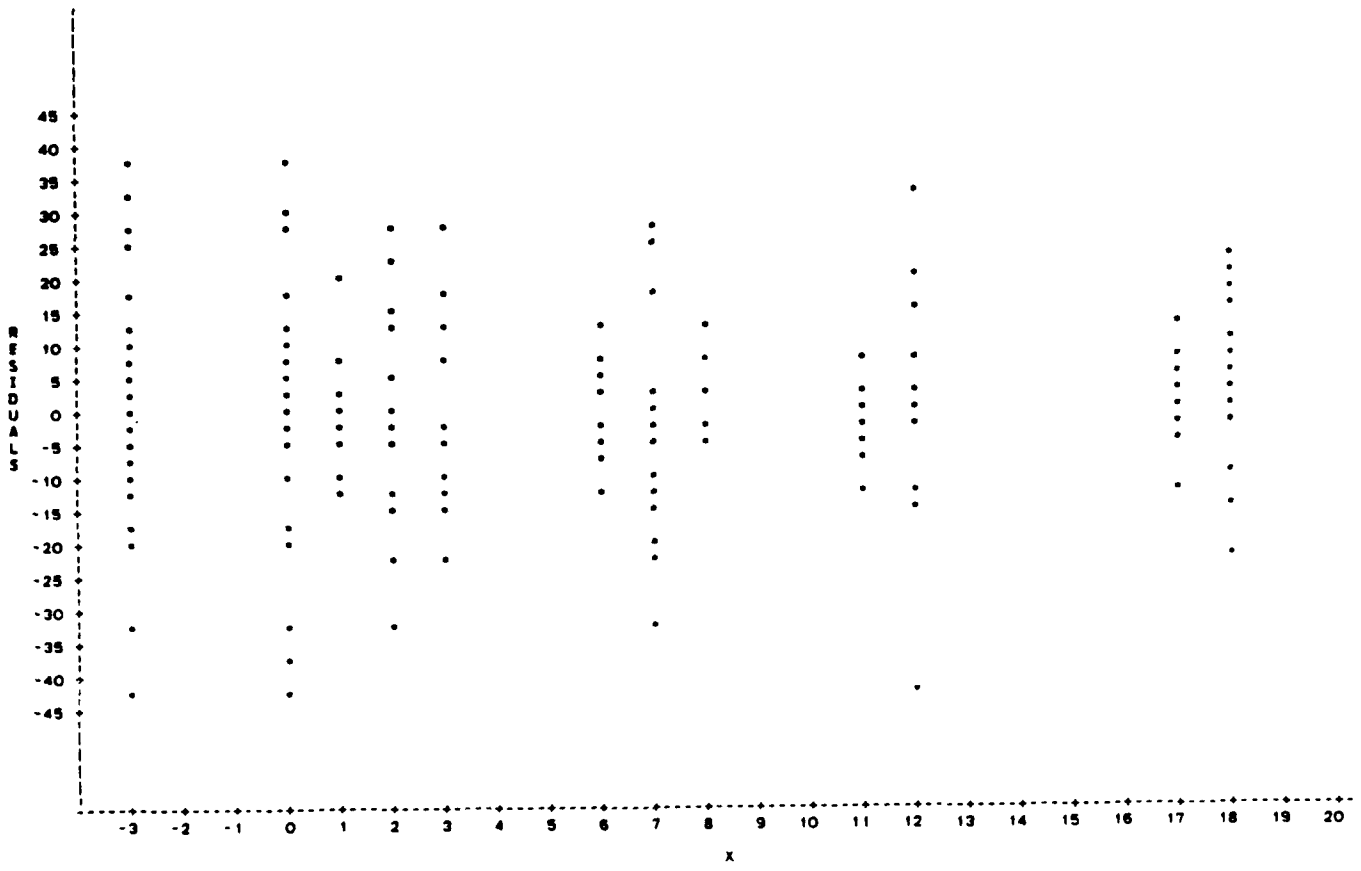
PARAMETER ESTIMATES

VARIABLE	DF	PARAMETER ESTIMATE	STANDARD ERROR	T FOR HO: PARAMETER=0	PROB > |T|
INTERCEP	1	373.70428	0.81793049	456.890	0.0001

this term contains both sum-of-squares pure error and sum-of-squares lack-of-fit.

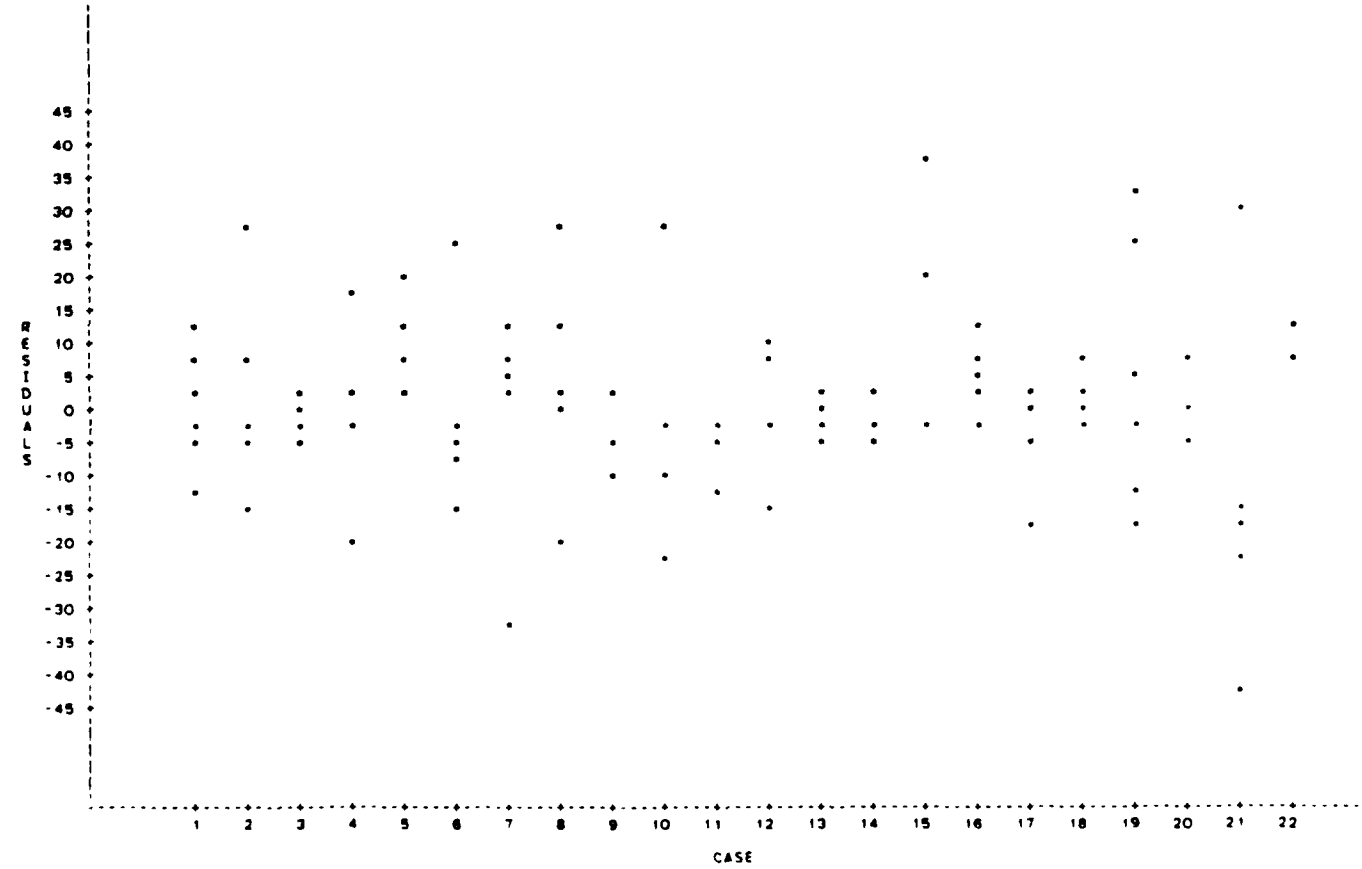
APPENDIX F

HEART RATE RESIDUAL PLOTS



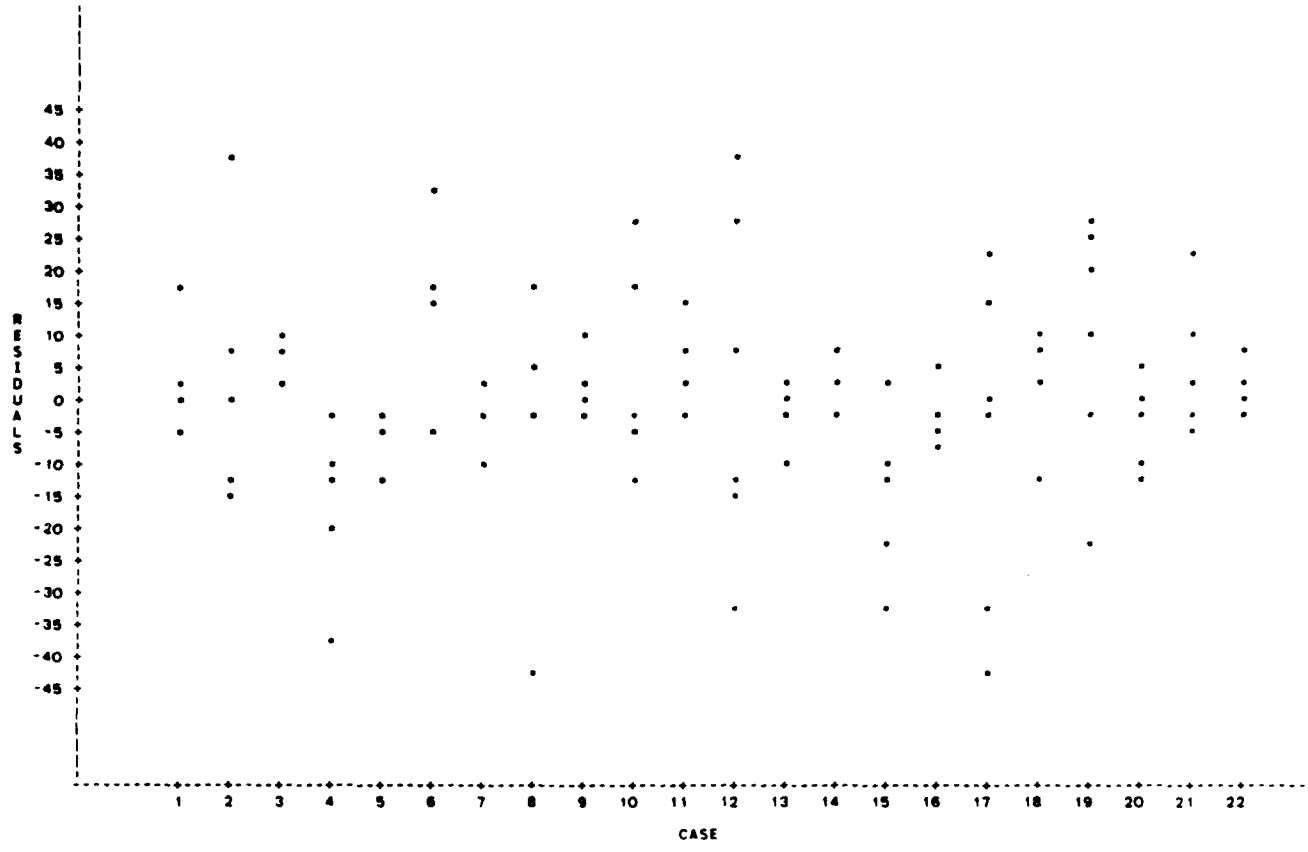
NOTE: 847 OBS HAD MISSING VALUES OR WERE OUT OF RANGE 125 OBS HIDDEN

Residuals versus time.



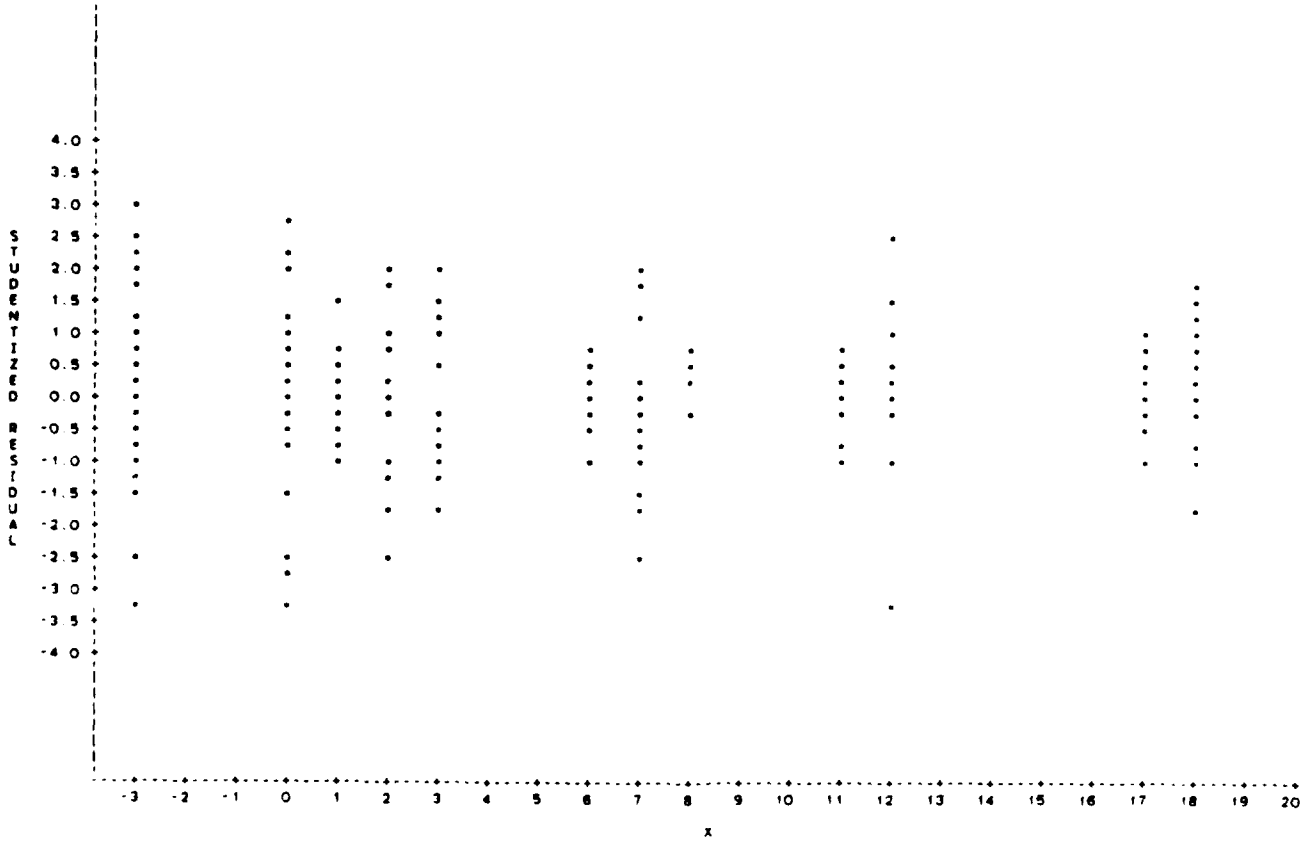
NOTE: 425 OBS HAD MISSING VALUES OR WERE OUT OF RANGE 36 OBS HIDDEN

Residuals versus animal ID number (sham-exposure group).



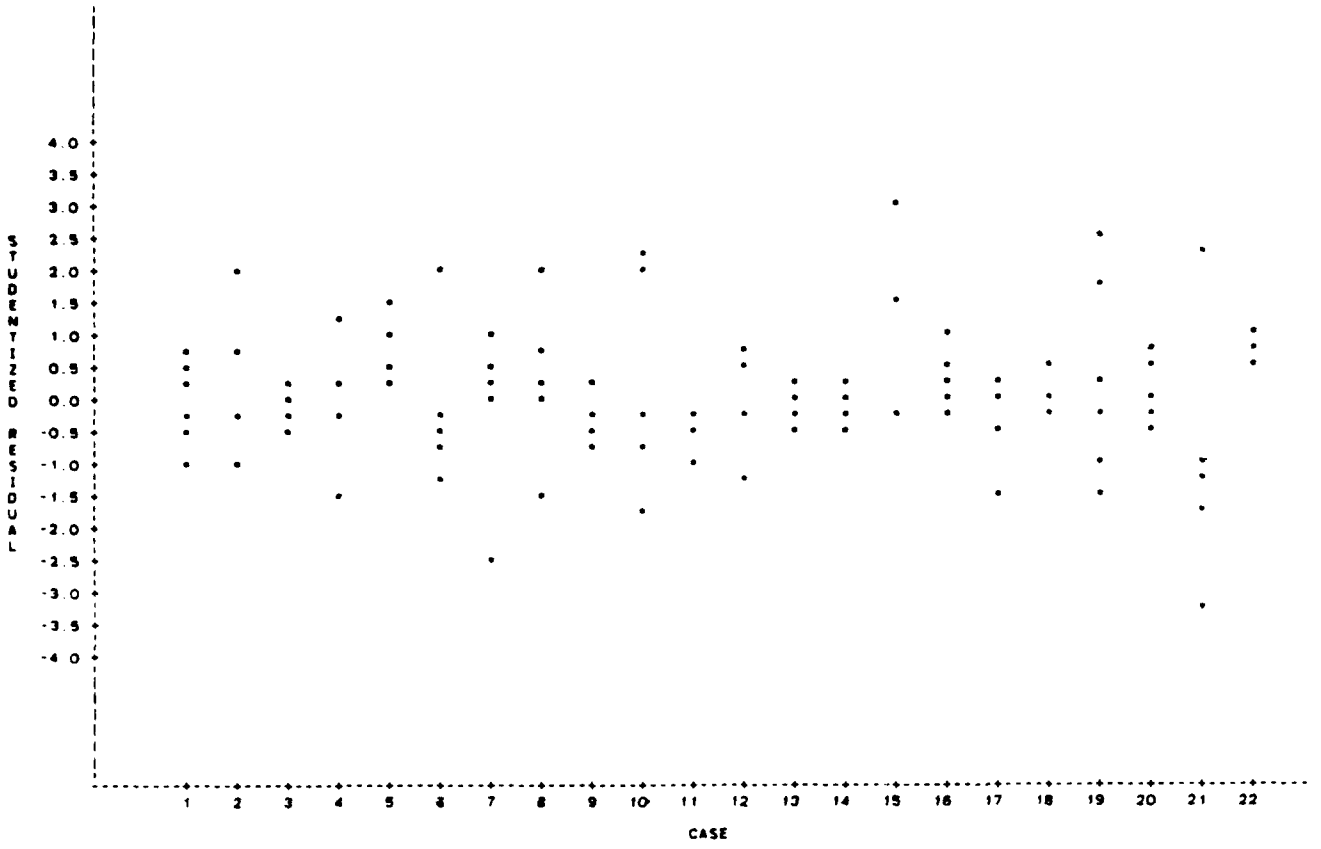
NOTE. 422 OBS HAD MISSING VALUES OR WERE OUT OF RANGE 34 OBS HIDDEN

Residuals versus animal ID number (exposure group).



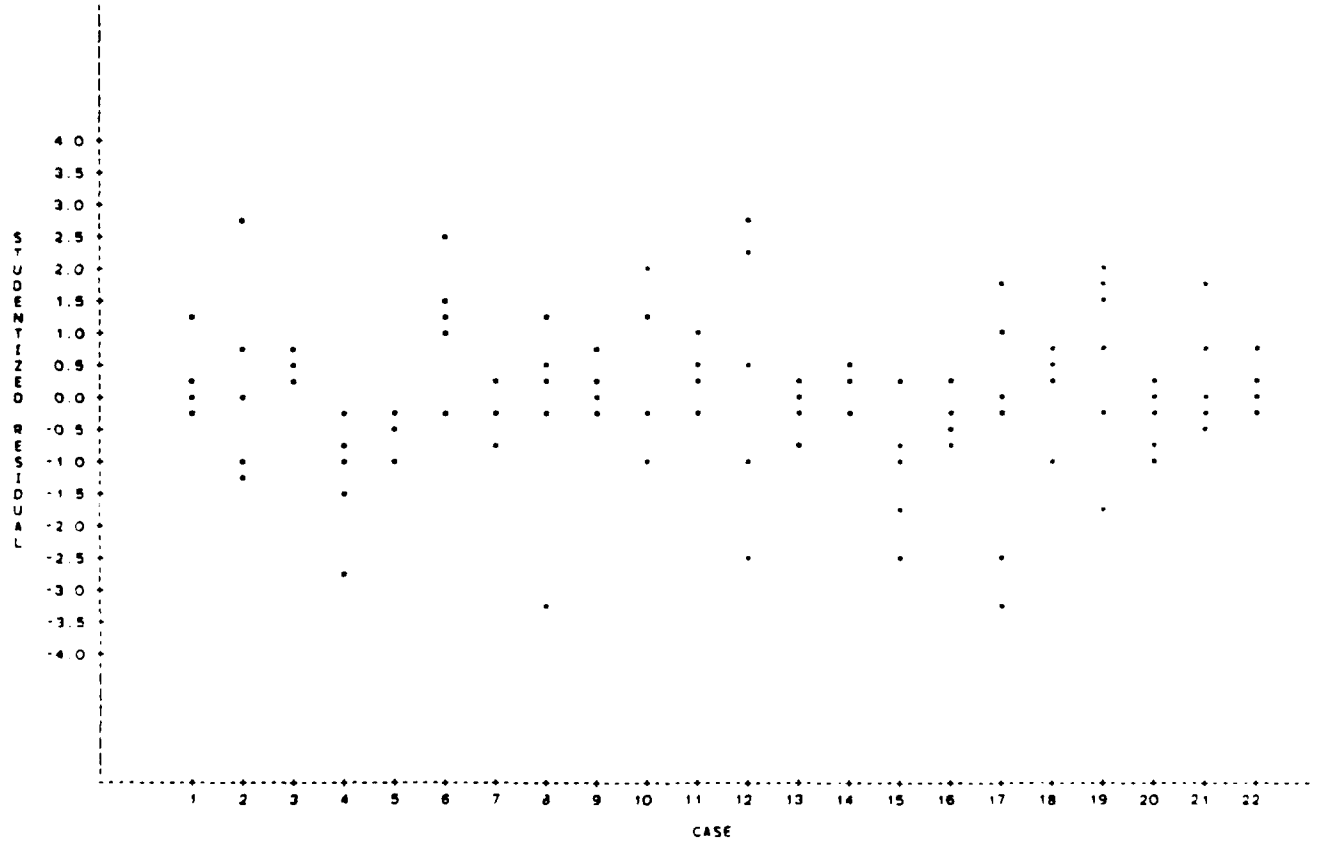
NOTE 847 OBS HAD MISSING VALUES OR WERE OUT OF RANGE 132 OBS HIDDEN

Studentized residuals versus time.



NOTE 425 OBS HAD MISSING VALUES OR WERE OUT OF RANGE 32 OBS HIDDEN

Studentized residuals versus animal ID number (sham-exposure group).



NOTE 422 OBS HAD MISSING VALUES OR WERE OUT OF RANGE 34 OBS HIDDEN

Studentized residuals versus animal ID number (exposure group).

APPENDIX G

RAW MEAN ARTERIAL BLOOD PRESSURE DATA SPREADSHEETS

Mean Arterial Blood Pressure (Controls I)

Rat #	Group	TIME -3WK	-2WK	0WK	1WK	2WK	3WK	4WK	5WK	6WK	7WK	8WK	9WK	10WK	11WK	12WK	13WK	14WK	15WK	16WK	17WK	18WK	19WK	20WK	2
1		112		108	116		108			[illegible]		120			103						107				
2		112		122		116					112					118									
3		116		118	108					114					114						[illegible]	112			
4		100		108		110					110					—						102			
5		119		116	116					118					[illegible]	116					124				
6		124		96			108				98					[illegible]						116			
7		118		116	[illegible]		116			119					108						[illegible]	110			
8		106		102		114						104				4					110				
9		118		116	116					107					[illegible]	114					115				
10		102		108			120				116											118			
11		118		115	[illegible]	116				106					116						108				
12		106		106		96						122				108						114			
13		[illegible]		112	116		118			[illegible]	110				114						115				

Mean Arterial Blood Pressure (Controls II)

Rat #	Group	TIME -3WK	-2WK	0WK	1WK	2WK	3WK	4WK	5WK	6WK	7WK	8WK	9WK	10WK	11WK	12WK	13WK	14WK	15WK	16WK	17WK	18WK	19WK	20WK
14		117		116	116					116					114						112			
15		102		108			103				110					100						108		
16		122		108	118					114					110						[illegible]			
17		106		98		100					108					—						112		
18		120		118	118					117					114						109			
19		114		102			104				110					108						110		
20		118		116	115					114					110						117			
21		102		108		106					106					112						98		
22		124		118	[illegible]	118				119					117						114			
23																								
24																								
25																								
26																								

Mean Arterial Blood Pressure (Microwaves I)

#	Group	-3WK	-2WK	0WK	TIME 1WK	2WK	3WK	4WK	5WK	6WK	7WK	8WK	9WK	10WK	11WK	12WK	13WK	14WK	15WK	16WK	17WK	18WK	19WK	20WK	2
		118		120	121		108			[illegible]		117			112						118				
		110		96		106					103					98									
		122		122	120					122					120						[illegible]	122			
		104		104		98					118					[illegible]						100			
		112		109	110					114					[illegible]	112					112				
		120		104			100				118											102			
		100		112	[illegible]	[illegible]	111			107					109						[illegible]	106			
		105		96		100						106									112				
		114		116	114					116					[illegible]	114					115				
		102		124			114				116											120			
		118		118	[illegible]	116				114					115						109				
		112		106		108						118				106						106			
		117		109	116		112			[illegible]	112				112						116				

Mean Arterial Blood Pressure (Microwaves II)

Rat #	Group	-3WK	-2WK	0WK	TIME 1WK	2WK	3WK	4WK	5WK	6WK	7WK	8WK	9WK	10WK	11WK	12WK	13WK	14WK	15WK	16WK	17WK	18WK	19WK	2
14		121		122	117					116					118						114			
15		101		102			100				102					100						102		
16		126		124	120					120					118						119			
17		98		102		104					108					110						105		
18		116		114	100					108					110						110			
19		114		104			122				119					116						120		
20		110		112	116					104					111						109			
21		110		104		112					116					102						114		
22		116		115	[illegible]	109				116					114						113			
23																								
24																								
25																								
26																								

APPENDIX H

MEAN ARTERIAL BLOOD PRESSURE
SAS FORMATTING PROGRAM

```
1          SAS(R) LOG  CMS SAS 5.16      VM/CMS CMS USER QSECLSB

NOTE: COPYRIGHT (C) 1984,1986 SAS INSTITUTE INC., CARY, N.C.  27511, U.S.A.
NOTE: CMS SAS RELEASE 5.16 AT GEORGIA INSTITUTE OF TECHNOLOGY (03559001).

NOTE: CPUID   VERSION = FF  SERIAL = 012242  MODEL = 4381 .

NOTE: SAS OPTIONS SPECIFIED ARE:
      LEAVE=0

  1 DATA TESTM;
  2 CMS FILEDEF X DISK MABP DAT A;
  3 CMS FILEDEF 20 DISK MABP0 LISTING A1 ( BLKSIZE 141 RECFM VBA LRECL 133;
  4 CMS FILEDEF 21 DISK MABP1 LISTING A1 ( BLKSIZE 141 RECFM VBA LRECL 133;
  5 CMS FILEDEF 22 DISK MABP2 LISTING A1 ( BLKSIZE 141 RECFM VBA LRECL 133;
  6 CMS FILEDEF 23 DISK MABP3 LISTING A1 ( BLKSIZE 141 RECFM VBA LRECL 133;
  7 CMS FILEDEF 24 DISK MABP4 LISTING A1 ( BLKSIZE 141 RECFM VBA LRECL 133;
  8 CMS FILEDEF 25 DISK MABP5 LISTING A1 ( BLKSIZE 141 RECFM VBA LRECL 133;
  9 CMS FILEDEF 26 DISK MABP6 LISTING A1 ( BLKSIZE 141 RECFM VBA LRECL 133;
 10 CMS FILEDEF 27 DISK MABP7 LISTING A1 ( BLKSIZE 141 RECFM VBA LRECL 133;
 11 ARRAY WEEK {24} WKN3 WKN2 MISSN1 WK0-WK20;
 12 KEEP X XSQR Y Z XZ XSQRZ CASE;
 13 INFILE X;
 14 INPUT CASE 1-3
 15       WKN3 5-7
 16       WKN2 9-11
 17       WK0 13-15
 18       WK1 17-19
 19       WK2 21-23
 20       WK3 25-27
 21       WK4 29-31
 22       WK5 33-35
 23       WK6 37-39
 24       WK7 41-43
 25       WK8 45-47
 26       WK9 49-51
 27       WK10 53-55
 28       WK11 57-59
 29       WK12 61-63
 30       WK13 65-67
 31       WK14 69-71
 32       WK15 73-75
 33       WK16 77-79
 34       WK17 81-83
 35       WK18 85-87
 36       WK19 89-91
 37       WK20 93-95
 38 ;
 39 MISSN1=.;
 40 IF CASE < 100 THEN Z = 0;
 41 IF CASE >= 100 THEN Z = 1;
 42 IF Z=1 THEN CASE=CASE-100;
 43 DO I = 1 TO 24;
 44 X = I-4; XSQR = X*X; XZ = X*Z; XSQRZ = X*X*Z; Y = WEEK {I};OUTPUT;
 45 END;


NOTE: INFILE X IS FILE MABP DAT A1
NOTE: 44 LINES WERE READ FROM INFILE X.
NOTE: DATA SET WORK.TESTM HAS 1056 OBSERVATIONS AND 7 VARIABLES.
```

```
2          SAS(R) LOG  CMS SAS 5.16      VM/CMS CMS USER QSECLSB

NOTE: THE DATA STATEMENT USED 0.36 SECONDS AND 332K.

 46 PROC CONTENTS;
NOTE: THE PROCEDURE CONTENTS USED 0.18 SECONDS AND 524K AND PRINTED PAGES 1 TO 2.

 47 PROC PRINTTO NEW UNIT=20;

NOTE: THE PROCEDURE PRINTTO USED 0.02 SECONDS AND 524K.

 48 PROC SORT OUT=SCTR;
 49       BY Z X Y;

NOTE: DATA SET WORK.SCTR HAS 1056 OBSERVATIONS AND 7 VARIABLES.
NOTE: THE PROCEDURE SORT USED 0.36 SECONDS AND 6924K.

 50 PROC SUMMARY;
 51       BY Z X;
 52       VAR Y;
 53       OUTPUT OUT=OVLMN MEAN=MEAN;
NOTE: THE DATA SET WORK.OVLMN HAS 48 OBSERVATIONS AND 5 VARIABLES.
NOTE: THE PROCEDURE SUMMARY USED 0.32 SECONDS AND 652K.

 54 DATA SMABP;
 55       SET SCTR OVLMN;
 56       BY Z;

NOTE: DATA SET WORK.SMABP HAS 1104 OBSERVATIONS AND 10 VARIABLES.
NOTE: THE DATA STATEMENT USED 0.31 SECONDS AND 588K.

 57 PROC PLOT NOLEGEND DATA=SMABP;
 58       BY Z;
 59       PLOT MEAN*X='X' Y*X='.' / VAXIS=75 TO 150 BY 10 OVERLAY;
 60       TITLE 'MEAN ARTERIAL BLOOD PRESSURE (mm Hg) SCATTER DIAGRAM';
NOTE: THE PROCEDURE PLOT USED 0.52 SECONDS AND 524K AND PRINTED PAGES 3 TO 4.

 61 PROC PRINTTO NEW UNIT=21;

NOTE: THE PROCEDURE PRINTTO USED 0.02 SECONDS AND 524K.

 62 PROC PLOT NOLEGEND DATA=SMABP;
 63       PLOT MEAN*X='X' / VAXIS=75 TO 150 BY 10;
 64       TITLE 'Mean Arterial Blood Pressure (in mm Hg) Versus Time';
NOTE: THE PROCEDURE PLOT USED 0.40 SECONDS AND 524K AND PRINTED PAGE 5.

 65 PROC PRINTTO NEW UNIT=22;
 66       TITLE 'ANIMAL MEAN ARTERIAL BLOOD PRESSURE ANALYSIS';

NOTE: THE PROCEDURE PRINTTO USED 0.03 SECONDS AND 524K.

 67 PROC DATASETS;
 68
LIST OF MEMBERS BEFORE UPDATE OF DIRECTORY.
NAME     MEMTYPE             OBS   TRACKS PROT
OVLMN    /DATA                48        1
SCTR     /DATA              1056        1
SMABP    /DATA              1104        1
TESTM    /DATA              1056        1
 68       DELETE SCTR;
```

```
 69      DELETE OVLMN;
 70      DELETE TESTM;
LIST OF MEMBERS AFTER UPDATE OF DIRECTORY.
NAME    MEMTYPE            OBS   TRACKS PROT
SMABP   /DATA             1104        1
NOTE: THE PROCEDURE DATASETS USED 0.13 SECONDS AND 588K.

 71 PROC STEPWISE DATA=SMABP;
 72      MODEL Y = X XSQR Z XZ XSQRZ / STEPWISE MAXR;
NOTE: THE PROCEDURE STEPWISE USED 0.30 SECONDS AND 588K AND PRINTED PAGES 6 TO 8.

 73 PROC PRINTTO NEW UNIT=23;

NOTE: THE PROCEDURE PRINTTO USED 0.02 SECONDS AND 524K.

 74 PROC REG;
 75      MODEL Y =  / PARTIAL;
 76      ID CASE;
ERROR: NEGATIVE SUM OF SQUARES REGRESSION ENCOUNTERED. HAVE YOU RESTRICTED THE INTERCEPT PAR
       NON-POSITIVE-DEFINITE CORRELATION OR SSCP MATRIX?
NOTE: ACOV AND SPEC OPTION ONLY VALID WITH RAWDATA
NOTE: THE PROCEDURE REG USED 0.53 SECONDS AND 780K AND PRINTED PAGES 9 TO 10.

 77 PROC PRINTTO NEW UNIT=24;

NOTE: THE PROCEDURE PRINTTO USED 0.02 SECONDS AND 524K.

 78 PROC GLM;
 79      CLASS X Z;
 80      MODEL Y = X Z X*Z;
NOTE: THE PROCEDURE GLM USED 1.30 SECONDS AND 1228K AND PRINTED PAGES 11 TO 12.

 81 PROC PRINTTO NEW UNIT=25;

NOTE: THE PROCEDURE PRINTTO USED 0.02 SECONDS AND 524K.

 82 PROC REG;
 83      MODEL Y =  / R;
 84      ID CASE;
 85      OUTPUT OUT=RMABP R=RESID STUDENT=STUDENT;
ERROR: NEGATIVE SUM OF SQUARES REGRESSION ENCOUNTERED. HAVE YOU RESTRICTED THE INTERCEPT PAR
       NON-POSITIVE-DEFINITE CORRELATION OR SSCP MATRIX?
NOTE: ACOV AND SPEC OPTION ONLY VALID WITH RAWDATA
NOTE: THE DATA SET WORK.RMABP HAS 1104 OBSERVATIONS AND 12 VARIABLES.
NOTE: THE PROCEDURE REG USED 2.13 SECONDS AND 780K AND PRINTED PAGES 13 TO 36.

 86 PROC PRINTTO NEW UNIT=26;

NOTE: THE PROCEDURE PRINTTO USED 0.02 SECONDS AND 524K.

 87 PROC PLOT DATA=RMABP;
 88      PLOT RESID*X='*' / VAXIS=-16.0 TO 16.0 BY 2.0;
 89      PLOT STUDENT*X='*' / VAXIS=-3.0 TO 3.0 BY 0.5;
 90      TITLE 'Mean arterial blood pressure residual plots';
NOTE: THE PROCEDURE PLOT USED 0.48 SECONDS AND 524K AND PRINTED PAGES 37 TO 38.

 91 PROC PRINTTO NEW UNIT=27;
```

```
4          SAS(R) LOG  CMS SAS 5.16       VM/CMS CMS USER QSECLSB

NOTE: THE PROCEDURE PRINTTO USED 0.02 SECONDS AND 524K.

 92 PROC PLOT DATA=RMABP;
 93      BY Z;
 94      PLOT RESID*CASE='*' / HAXIS=1 TO 22 BY 1 VAXIS=-16.0 TO 16.0 BY 2.0;
 95      PLOT STUDENT*CASE='*' / HAXIS=1 TO 22 BY 1 VAXIS=-3.0 TO 3.0 BY 0.5;
 96      TITLE 'Mean arterial blood pressure residual plots';
NOTE: THE PROCEDURE PLOT USED 0.45 SECONDS AND 524K AND PRINTED PAGES 39 TO 42.
NOTE: SAS USED 6924K MEMORY.

ERROR: ERRORS ON PAGES 3.

NOTE: SAS INSTITUTE INC.
      SAS CIRCLE
      PO BOX 8000
      CARY, N.C. 27511-8000
```

APPENDIX I

STEPWISE AND MAXIMUM R^2 REGRESSION PROCEDURES USED TO BUILD MEAN ARTERIAL BLOOD PRESSURE MODEL

ANIMAL MEAN ARTERIAL BLOOD PRESSURE ANALYSIS 17:58 THURSDAY, FEBRUARY 19, 1987

STEPWISE REGRESSION PROCEDURE FOR DEPENDENT VARIABLE Y

WARNING: 847 OBSERVATIONS DELETED DUE TO MISSING VALUES.

NOTE: SLENTRY AND SLSTAY HAVE BEEN SET TO .15 FOR THE STEPWISE TECHNIQUE.

NO VARIABLES MET THE 0.1500 SIGNIFICANCE LEVEL FOR ENTRY INTO THE MODEL.

ANIMAL MEAN ARTERIAL BLOOD PRESSURE ANALYSIS 17:58 THURSDAY, FEBRUARY 19, 1987

MAXIMUM R-SQUARE IMPROVEMENT FOR DEPENDENT VARIABLE Y

WARNING: 847 OBSERVATIONS DELETED DUE TO MISSING VALUES.

STEP 1 VARIABLE X ENTERED R SQUARE = 0.00130964 C(P) = -1.25172554

	DF	SUM OF SQUARES	MEAN SQUARE	F	PROB>F
REGRESSION	1	15.27517127	15.27517127	0.33	0.5636
ERROR	255	11648.39798048	45.67999208		
TOTAL	256	11663.67315175			

	B VALUE	STD ERROR	TYPE II SS	F	PROB>F
INTERCEPT	112.04473938				
X	-0.03494094	0.06042331	15.27517127	0.33	0.5636

BOUNDS ON CONDITION NUMBER: 1, 1

THE ABOVE MODEL IS THE BEST 1 VARIABLE MODEL FOUND.

STEP 2 VARIABLE Z ENTERED R SQUARE = 0.00253582 C(P) = 0.43918118

	DF	SUM OF SQUARES	MEAN SQUARE	F	PROB>F
REGRESSION	2	29.57692377	14.78846188	0.32	0.7244
ERROR	254	11634.09622798	45.80352846		
TOTAL	256	11663.67315175			

	B VALUE	STD ERROR	TYPE II SS	F	PROB>F
INTERCEPT	112.28088874				
X	-0.03481651	0.06050537	15.16636892	0.33	0.5655
Z	-0.47180690	0.84434343	14.30175250	0.31	0.5768

BOUNDS ON CONDITION NUMBER: 1.000014, 4.000054

THE ABOVE MODEL IS THE BEST 2 VARIABLE MODEL FOUND.

STEP 3 VARIABLE XZ ENTERED R SQUARE = 0.00317290 C(P) = 2.27858643

	DF	SUM OF SQUARES	MEAN SQUARE	F	PROB>F
REGRESSION	3	37.00764632	12.33588211	0.27	0.8488
ERROR	253	11626.66550543	45.95519963		
TOTAL	256	11663.67315175			

	B VALUE	STD ERROR	TYPE II SS	F	PROB>F
INTERCEPT	112.41233558				
X	-0.05927174	0.08585863	21.90090632	0.48	0.4906
Z	-0.73503589	1.06948421	21.70715923	0.47	0.4925
XZ	0.04874079	0.12121166	7.43072255	0.16	0.6879

BOUNDS ON CONDITION NUMBER: 2.611822, 18.65386

MAXIMUM R-SQUARE IMPROVEMENT FOR DEPENDENT VARIABLE Y

THE ABOVE MODEL IS THE BEST 3 VARIABLE MODEL FOUND.

STEP 4 VARIABLE XSQR ENTERED R SQUARE = 0.00337989 C(P) = 4.22640916

	DF	SUM OF SQUARES	MEAN SQUARE	F	PROB>F
REGRESSION	4	39.42188962	9.85547241	0.21	0.9307
ERROR	252	11624.25126213	46.12798120		
TOTAL	256	11663.67315175			

	B VALUE	STD ERROR	TYPE II SS	F	PROB>F
INTERCEPT	112.41405165				
X	-0.09374800	0.17352166	13.46421564	0.29	0.5895
XSQR	0.00236609	0.01034244	2.41424330	0.05	0.8192
Z	-0.73488836	1.07149303	21.69843862	0.47	0.4934
XZ	0.04881544	0.12143975	7.45344577	0.16	0.6880

BOUNDS ON CONDITION NUMBER: 8.166951, 78.09775

THE ABOVE MODEL IS THE BEST 4 VARIABLE MODEL FOUND.

STEP 5 VARIABLE XSQRZ ENTERED R SQUARE = 0.00427806 C(P) = 6.00000000

	DF	SUM OF SQUARES	MEAN SQUARE	F	PROB>F
REGRESSION	5	49.89784635	9.97956927	0.22	0.9540
ERROR	251	11613.77530540	46.27002114		
TOTAL	256	11663.67315175			

	B VALUE	STD ERROR	TYPE II SS	F	PROB>F
INTERCEPT	112.41763379				
X	-0.16571397	0.23038542	23.93910614	0.52	0.4726
XSQR	0.00730508	0.01466414	11.48251492	0.25	0.6188
Z	-0.74234448	1.07325586	22.13625390	0.48	0.4898
XZ	0.19229433	0.32514268	16.18395679	0.35	0.5548
XSQRZ	-0.00985754	0.02071675	10.47595673	0.23	0.6346

BOUNDS ON CONDITION NUMBER: 18.66541, 334.4465

THE ABOVE MODEL IS THE BEST 5 VARIABLE MODEL FOUND.

APPENDIX J

MEAN ARTERIAL BLOOD PRESSURE LACK-OF-FIT TEST

ANIMAL MEAN ARTERIAL BLOOD PRESSURE ANALYSIS 15:58 TUESDAY, APRIL 14, 1987

GENERAL LINEAR MODELS PROCEDURE

DEPENDENT VARIABLE: Y

SOURCE	DF	SUM OF SQUARES	MEAN SQUARE	F VALUE	PR > F	R-SQUARE
MODEL	23	1288.52163660	56.02267985	1.26	0.1981	0.110473
ERROR	233	10375.15151515	44.52854728		ROOT MSE	
CORRECTED TOTAL	256	11663.67315175			6.67297140	

SOURCE	DF	TYPE I SS	F VALUE	PR > F	DF	TYPE III SS	F VALUE
X	11	1066.32805796	2.18	0.0164	11	1055.46332294	2.15
Z	1	13.06280920	0.29	0.5886	1	16.25400790	0.37
X*Z	11	209.13076944	0.43	0.9431	11	209.13076944	0.43

this term is solely a measure of sum-of-squares pure error.

Partitioning SS_E into SS_{pe} and SS_{lof}

$SS_E = 11663.6732$ df = 256

$SS_{pe} = 10375.1515$ df = 233

$SS_{lof} = 1288.5216$ df = 23

$MS_{lof} = 56.0227$

$MS_{pe} = 44.5285$

$$F_o = \frac{MS_{lof}}{MS_{pe}} = 1.2581$$

$F_{0.10,23,233} \sim 1.22$

$\therefore$ model fit is acceptable.

ANIMAL MEAN ARTERIAL BLOOD PRESSURE ANALYSIS

ANALYSIS OF VARIANCE

SOURCE	DF	SUM OF SQUARES	MEAN SQUARE	F VALUE	PROB>F
MODEL	0	-2.32831E-10			
ERROR	256	11663.67315	45.56122325		
C TOTAL	256	11663.67315			

ROOT MSE		R-SQUARE	-0.0000
DEP MEAN	111.856	ADJ R-SQ	-0.0000
C.V.			

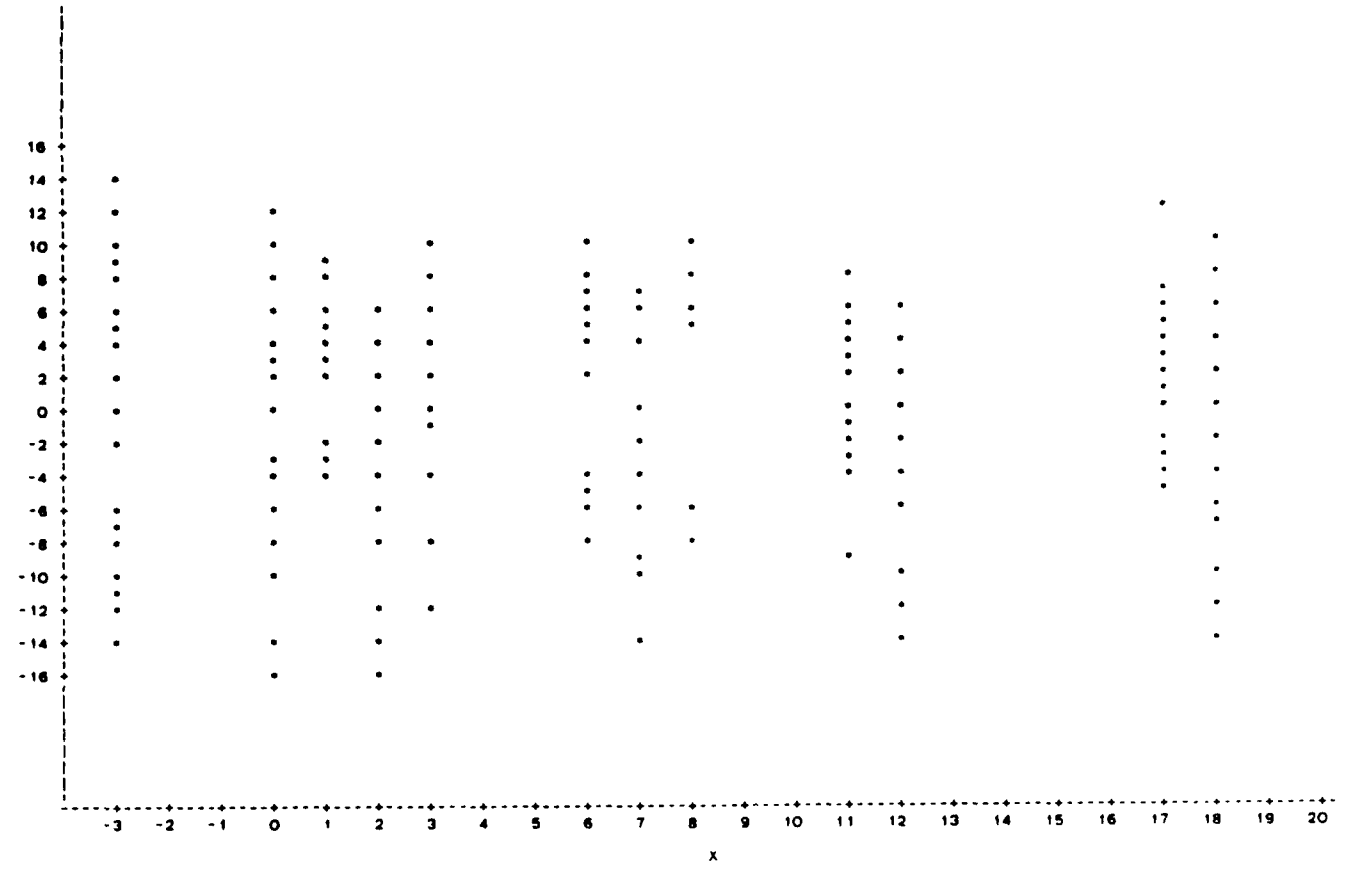
PARAMETER ESTIMATES

VARIABLE	DF	PARAMETER ESTIMATE	STANDARD ERROR	T FOR HO: PARAMETER=0	PROB > |T|
INTERCEP	1	111.85603	0.42104753	265.661	0.0001

this term contains both sum-of-squares pure error and sum-of-squares lack-of-fit.

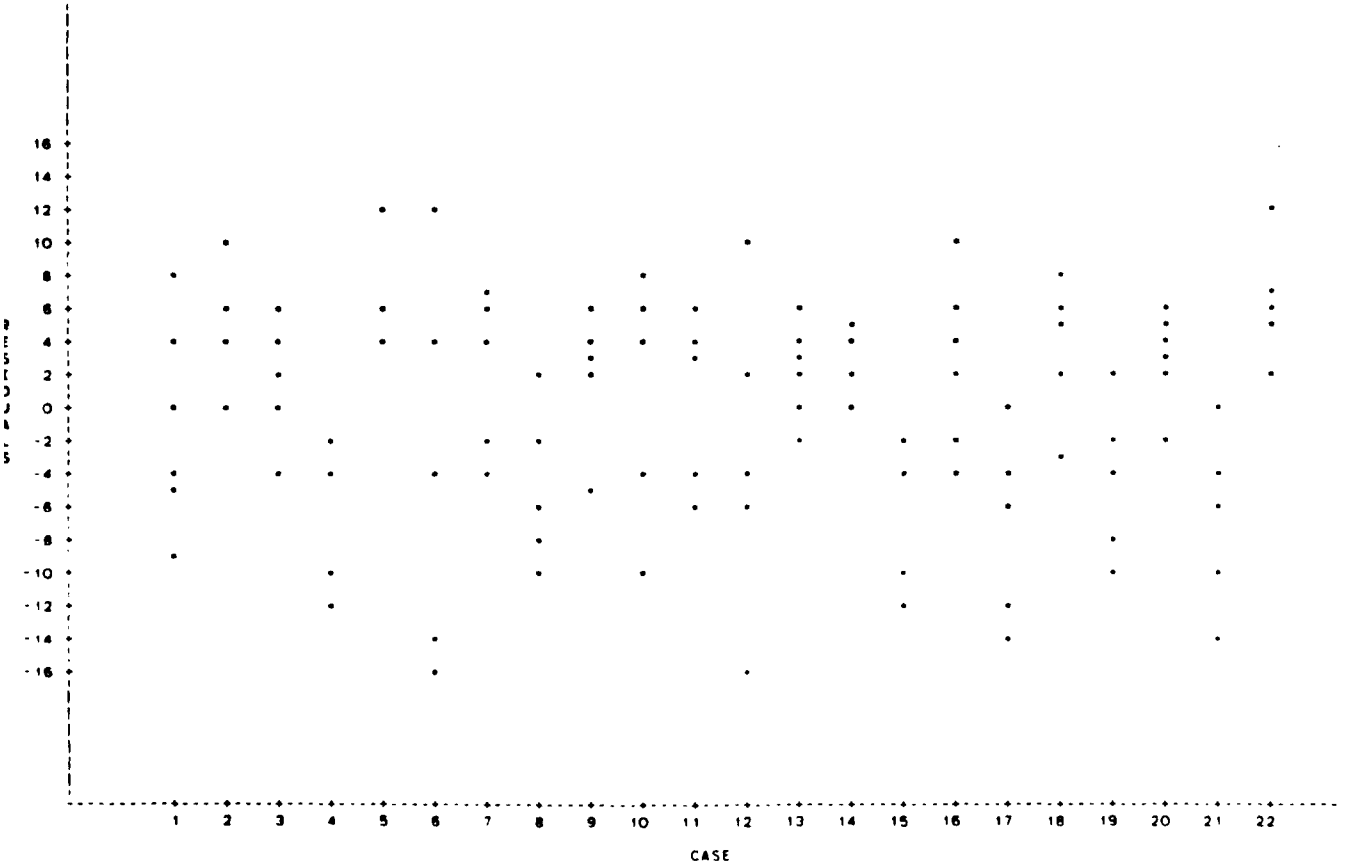
APPENDIX K

MEAN ARTERIAL BLOOD PRESSURE RESIDUAL PLOTS



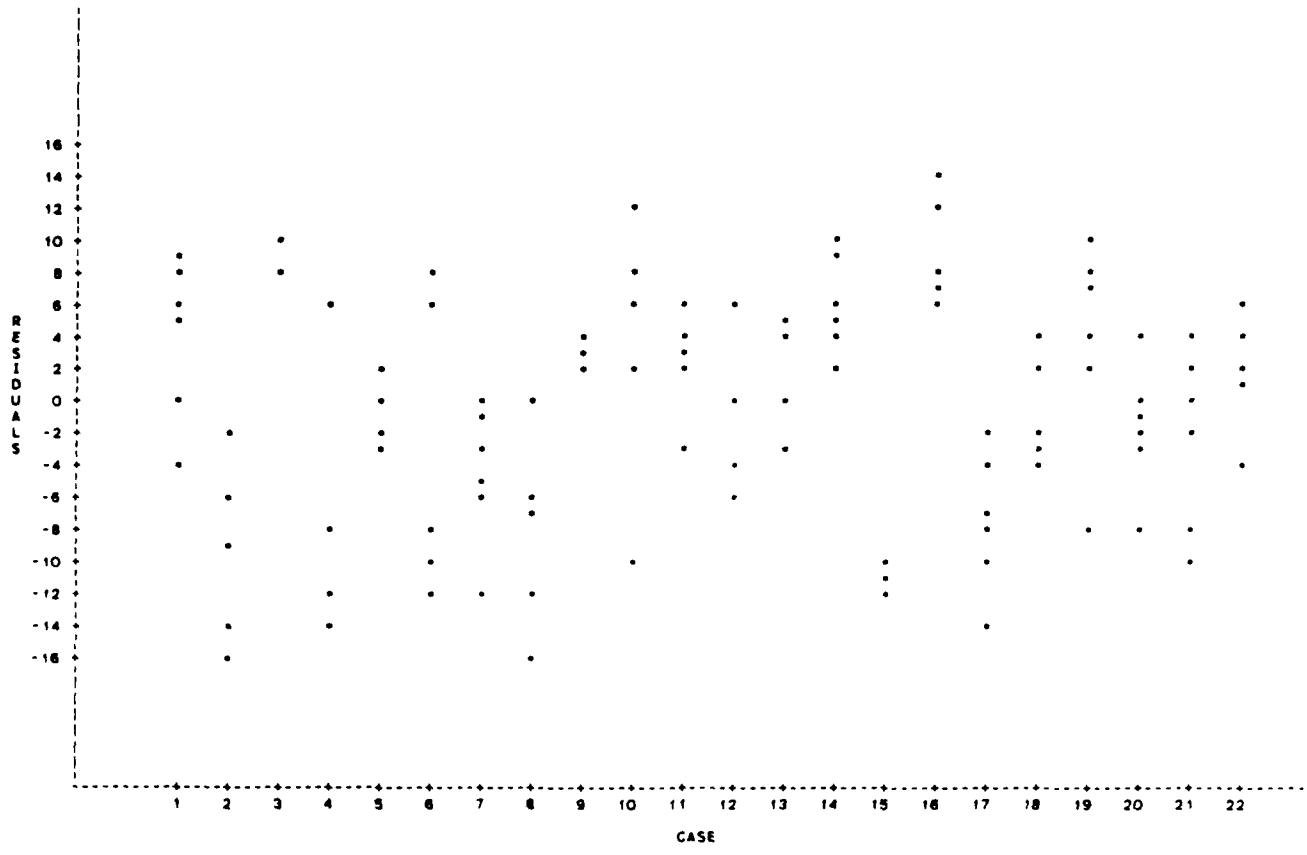
NOTE: 848 OBS HAD MISSING VALUES OR WERE OUT OF RANGE 117 OBS HIDDEN

Residuals versus time.



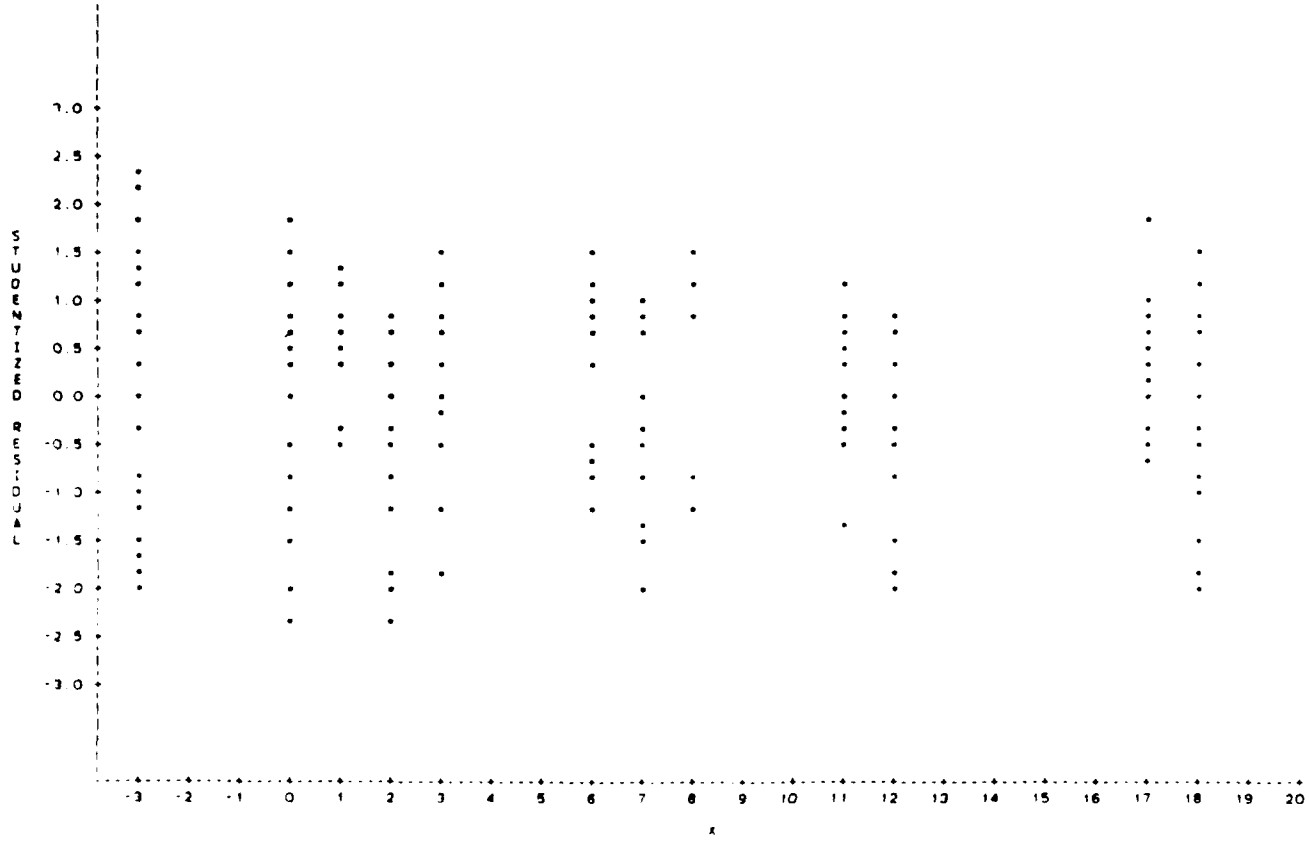
NOTE 425 OBS HAD MISSING VALUES OR WERE OUT OF RANGE 19 OBS HIDDEN

Residuals versus animal ID number (sham-exposure group).



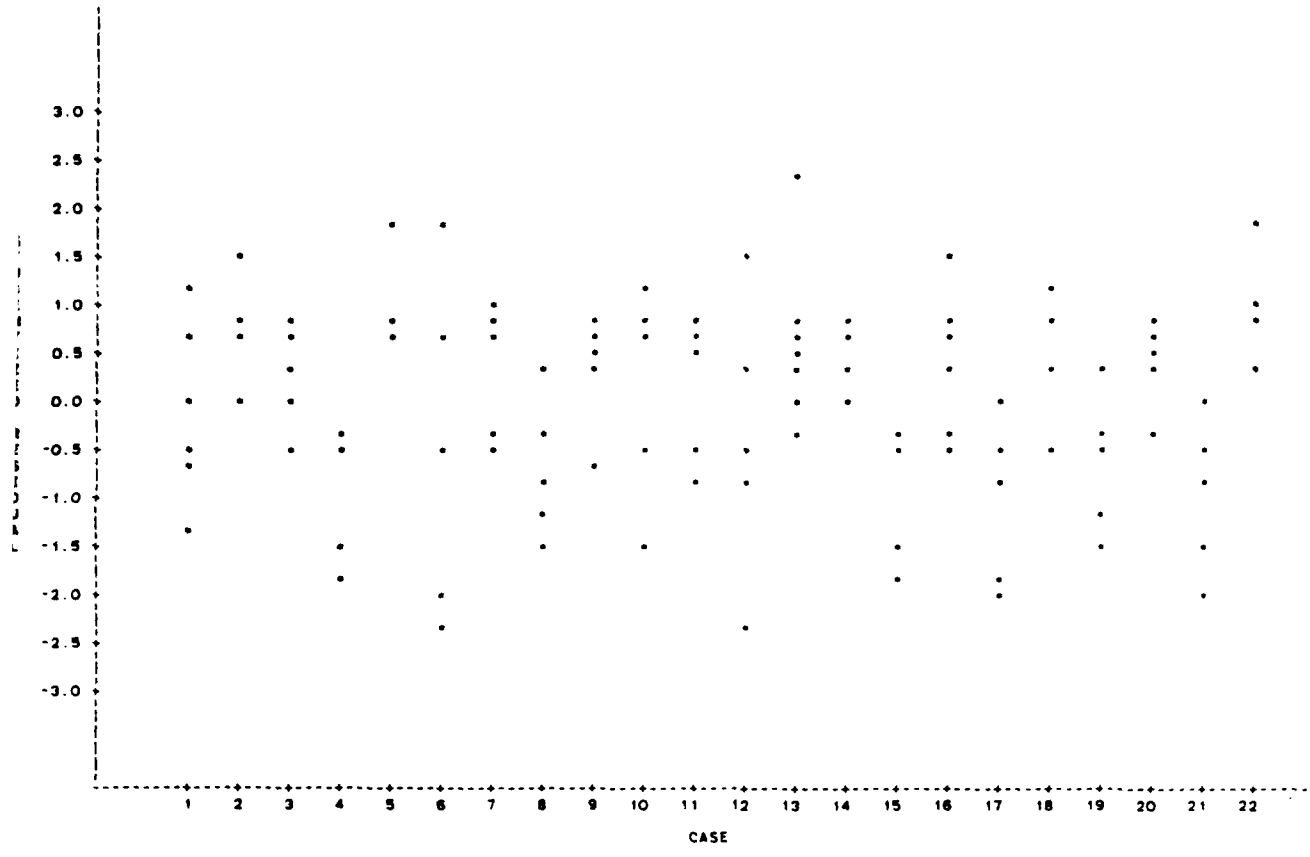
NOTE: 423 OBS HAD MISSING VALUES OR WERE OUT OF RANGE 23 OBS HIDDEN

Residuals versus animal ID number (exposure group).



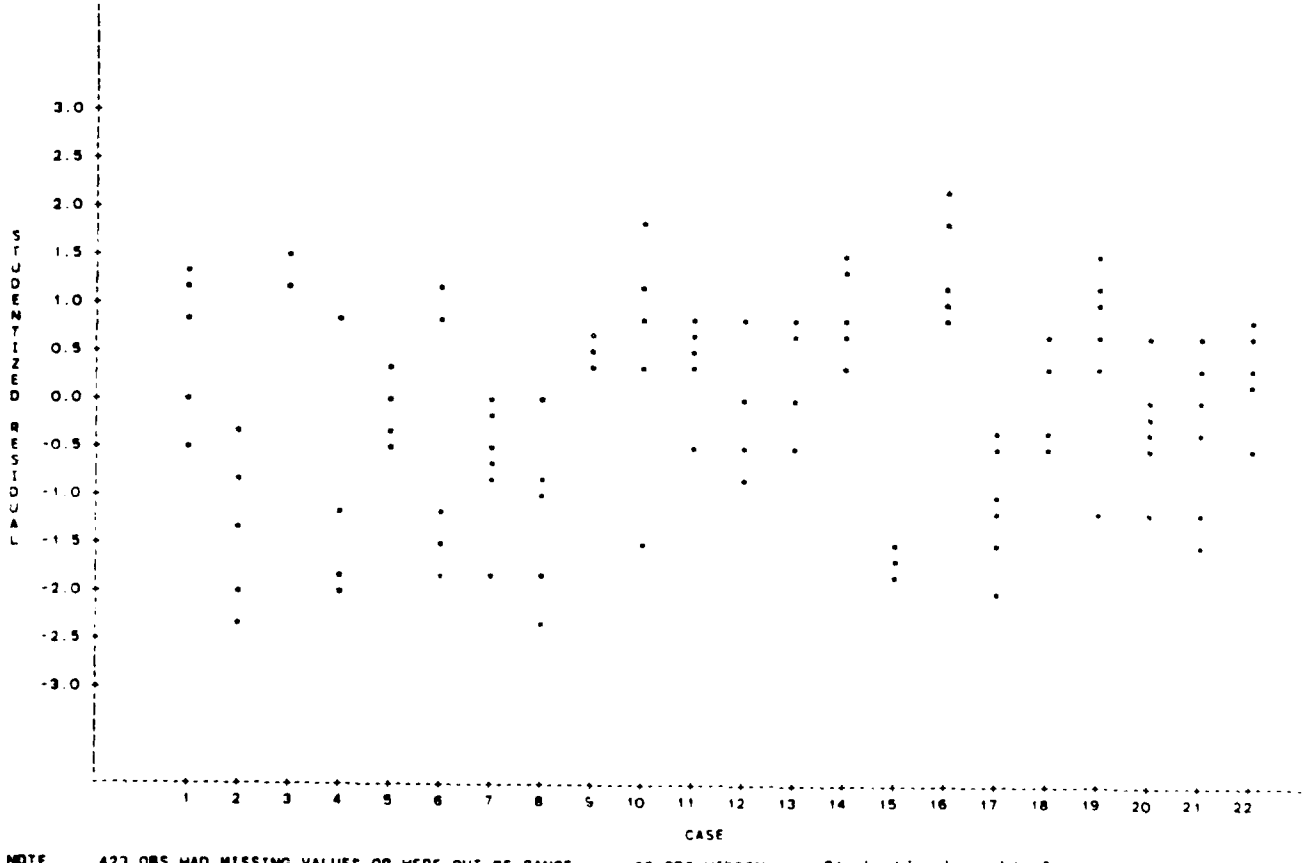
NOTE 847 OBS HAD MISSING VALUES OR WERE OUT OF RANGE 127 OBS HIDDEN

Studentized residuals versus time.



NOTE: 424 OBS HAD MISSING VALUES OR WERE OUT OF RANGE 22 OBS HIDDEN

Studentized residuals versus animal ID number (sham-exposure group).



NOTE 423 OBS HAD MISSING VALUES OR WERE OUT OF RANGE 26 OBS HIDDEN

Studentized residuals versus animal ID number (exposure group).

END

DATE

FILMED

6-1988

DTIC